January 19, 2001

MEMORANDUM

SUBJECT: **ATRAZINE**. HED's Revised Preliminary Human Health Risk Assessment for the Reregistration Eligibility Decision (RED). DP Barcode: D272009. PC Code: 080803. Case No. 0062.

FROM: Catherine Eiden, Senior Scientist
Reregistration Branch 3
Health Effects Division (7509C)

TO: Pam Noyes, Special Review Manager
Special Review and Reregistration Division (7508C)

This memorandum, the accompanying human health risk assessment and attachments serve as the HED Revised Preliminary Human Health Risk Assessment for the RED for atrazine. The attachments include: 1) HED Toxicology Chapter dated 01/18/01, L Taylor & R. Hawks (Attachment I), 2) Report of the Hazard Identification Assessment Review Committee (HIARC) memoranda dated 12/21/00, V. Dellarco and K. Baetcke (Attachment II), 3) FQPA Safety Factor Recommendations (11/14/00), B. Tarplee (Attachment III), 4) HED Product and Residue Chemistry Chapter dated 01/18/01, C. Eiden and D. Soderberg (Attachment IV), 5) Anticipated Residues and Acute and Chronic Dietary Exposure Assessments for Atrazine dated 01/18/01, C. Eiden and D. Soderberg (Attachment V), 6) HED Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Atrazine dated 01/18/01, G. Bangs (Attachment VI), 7) EFED Drinking Water Exposure Assessment, J. Lin, H. Nelson, and M. Frankenberry (Attachment VII), and 8) Review of Atrazine Incident Reports, J. Blondell (Attachment VIII). These attachments contain the basic information used here to describe the overall exposure and risk estimates associated with the use of atrazine. Cumulative risk assessment, which considers risks from other pesticides which have a common mechanism of toxicity is not addressed in this document.

This document contains revisions to the preliminary human health risk assessment dated November 30,

2000 made in response to the Phase I Review 30-day registrant error correction.

HED notes that the following raw agricultural commodities were excluded from the preliminary dietary risk assessments for atrazine because there is no reasonable expectation of residues in these commodities: secondary residues in poultry meat, fat, and meat byproducts and eggs, and meat, fat, and meat byproducts of hogs.

To date, HED has conducted drinking water exposure assessments for pesticides using screening-level water quality models for the most part. However, there are more data available to assess exposures to atrazine in finished drinking than for any other pesticide. For this reason, monitoring data on actual residues of atrazine in finished drinking water have been used for this assessment in lieu of the screening-level water quality models usually employed. Because of the volume of information available through various data sets for thousands of community water systems and hundreds of rural wells, HED has developed a methodology by which the data have been used initially in a deterministic assessment of exposure. Community water systems identified under the deterministic approach as having exposures above HED's level of concern, will be assessed under a probabilistic approach making use of all distributions of data available on drinking water consumption, body weight, and atrazine residues in finished drinking water. Because of the time constraints on this risk assessment, this document contains only the results of the deterministic assessment of drinking water exposure for atrazine. Future revisions to the drinking water exposure assessment should include probabilistic assessments of drinking water exposure for those community water systems found to have concentrations of atrazine residues above HED's level of concern under the deterministic assessment presented in this document.

REVISED PRELIMINARY HUMAN HEALTH RISK ASSESSMENT
ATRAZINE

January 19, 2001
Reregistration Branch 3
Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency

TABLE OF CONTENTS

1.0 Executive Summary 5

2.0 Physical and Chemical Properties Characterization 26

3.0 Hazard Characterization 27
3.1 Hazard Profile 27
3.2 FQPA Considerations 31
3.3 Dose Response Assessment 32
3.3.1 Atrazine and the Chlorinated Metabolites 33
3.3.2 Hydroxyatrazine 42

4.0 Exposure Assessment 45
4.1 Summary of Registered Uses 45
4.2 Dietary Exposure 47
4.2.1 Food Exposure 47
4.2.2 Drinking Water Exposure 60
4.3 Occupational Exposure 85
4.3.1 Handler 86
4.3.2 Post application 99
4.4 Residential Exposure 104
4.4.1 Handler 104
4.4.2 Post application 108

5.0 Aggregate Risk Assessments and Risk Characterization 112

6.0 Data Requirements 116

1.0 EXECUTIVE SUMMARY

Background

This document contains the Health Effects Division's (HED's) revised preliminary human health risk assessment for atrazine. HED is providing this document in support of the reregistration eligibility decision for atrazine, and to conclude the special review on atrazine. The risk estimates provided in this document are subject to revision once the general public has had the opportunity to review and comment on these preliminary results.

Atrazine, a systemic herbicide that blocks photosynthesis, is currently one of the two most widely used agricultural pesticides in the U.S. Approximately 64 to 75 million pounds (lbs) of active ingredient (a.i.) are applied per year. About three-fourths of all field corn and sorghum are treated with atrazine annually for weed control. Seventy percent (70%) of the atrazine applied to corn and sorghum is used prior to emergence (pre-emergence), and thirty percent (30%) is applied post-emergence.

Atrazine is metabolized to four hydroxyatrazine compounds and to three chlorinated atrazine compounds, and conjugates of these compounds. The hydroxy compounds are the dominate metabolites found in plants, while the chlorinated compounds (desethylated atrazine, desisopropyl atrazine, and diaminochlorotriazine (DACT)) dominate in animal tissues, and in soils and water.

Atrazine is the most commonly detected pesticide in ground and surface water. It has been the subject of multiple monitoring programs conducted by the registrant, academia, states, and government agencies, in particular the U.S. Geological Survey (USGS). Atrazine's frequent detection in streams, rivers, groundwater, and reservoirs is related directly to both its volume of usage, and its tendency to persist in soils and move with water.

Regulatory History

Atrazine's unique regulatory history began in the early 1990s. Atrazine's occurrence in the environment prompted the Environmental Protection Agency's (EPA or the Agency) Office of Water (OW) to regulate atrazine under the Safe Drinking Water Act (SDWA), and in 1991 OW established a Maximum Contaminant Level (MCL) of 3 parts per billion (ppb) for atrazine. Under the SDWA, atrazine has been subject to compliance monitoring. OW has also established a one-day Health Advisory Level (HAL) for atrazine of 100 ppb. Prior to EPA initiating a Special Review, the registrant voluntarily instituted several risk reduction measures to address concerns raised about surface water and groundwater contamination by atrazine. In 1990, the following measures were undertaken by the registrant to address groundwater exposure concerns:

- Reduction of the application rate for corn and sorghum to 3.0 lbs a.i./acre from 4.0 lbs a.i./acre.

- Classification of all atrazine-containing products (except for the lawn care, turf, and conifer uses) as Restricted Use Pesticides (RUPs).
- Institution of a well-head protection plan requiring 50 foot setbacks around all wells for mixing, loading, or applying atrazine-containing products.
- Deletion of most non-crop land uses that typically had high application rates, such as industrial sites, medians, railroad rights-of-way, and non-crop areas of farms.
- Prohibition of chemigation (applying atrazine through irrigation systems).

In 1992, the following additional measures were undertaken to address concerns about atrazine contamination of surface water sources:

- Further reduction of the total seasonal application rates for corn and sorghum to 2.5 lbs a.i./acre per year. This rate includes a 1.5 lbs a.i./acre per year pre-emergence use and a 1.0 lbs a.i./acre per year post-emergence use.

- Expansion of the setback requirements, including: a 50 foot setback around surface water sources when workers are mixing and loading atrazine-containing products; a 66 foot application (ground and aerial) setback from points of entry where field surface water runoff enters surface water sources; and, a 200 foot application setback around lakes and reservoirs.

- Institution of construction requirements for bulk storage facilities to eliminate point source contamination from spills.

In November 1994, EPA initiated a Special Review for the Triazine pesticides, atrazine, simazine and cyanazine, based on cancer risk concerns for people potentially exposed to atrazine through consumption of food and drinking water, and lawn treatments. The basis for the Special Review also included cancer risk concerns for workers exposed to atrazine in various agricultural settings and application scenarios. At the time that the Special Review was initiated, atrazine and the other Triazines were classified as Group C carcinogens (possible human carcinogens) based on an increase in tumors in laboratory animals, and the potential cancer potency was quantified for atrazine and the other Triazines using a linearized, low-dose extrapolation model (Q_1^*).

Atrazine is still subject to the conditions of the Special Review and is undergoing reregistration and tolerance reassessment under the Food Quality Protection Act (FQPA). In addition, atrazine and the other Triazines are included in priority Group 1 for the purpose of tolerance reassessment. Since the Special Review was initiated, EPA has received and reviewed a large volume of new data on atrazine, including new toxicology data on the mode of action leading to early onset of mammary tumors in the Sprague-Dawley strain of rat, and substantial amounts of drinking water monitoring data. Based on the refinements to and completeness of the atrazine database, the Agency believes it is now appropriate to prepare a revised preliminary human health risk assessment for atrazine. However, the Agency is still

awaiting the submission of additional data relevant to toxicity issues and residues in drinking water that will allow the Agency to further refine its risk estimates and clarify uncertainties associated with the risk estimates.

Currently registered uses of atrazine

Atrazine is an herbicide registered for the control of broadleaf weeds and some grassy weeds. Atrazine is currently used on corn (field and sweet), sorghum, sugarcane, wheat (where application is to wheat stubble on fallow land following wheat harvests; wheat is not the target crop), guava, macadamia nuts, orchard grass and hay, range grasses, and southern turf grasses. Atrazine is most widely used on corn followed by use on sorghum and sugarcane. The uses on orchard grass and hay are not supported by the primary producer, and HED is recommending the revocation of the orchard grass and hay tolerances.

Atrazine is registered for use on range grasses for the establishment of permanent grass cover on rangelands and pastures under the Conservation Reserve Program (CRP) in four states: OK, NE, TX, and OR. The CRP is administered by the U.S. Department of Agriculture (USDA). There are prohibitions against grazing on these CRP lands, and cutting the grasses for hay, except in national emergencies, such as severe drought. However, if atrazine is used on CRP lands for establishment of permanent grasses, grazing and harvesting hay for feed are prohibited. There are also "right-of-way" uses with grazing restrictions. Atrazine is also registered for use on the following non-agricultural use sites: lawns, golf courses, and sod farms. Atrazine is formulated variously as dry flowables, and water-based flowable formulations.

Potential sources of exposure to atrazine

HED has considered potential exposure pathways based on atrazine's use pattern as described above. Atrazine’s physical/chemical properties affect the fate and transport of the compound and its availability in the environment, in edible portions of plants, in water used for drinking, and on treated foliage. It is generally accepted that atrazine's relative persistence and mobility in the environment coupled with its widespread use on animal feed crops (corn) result in the frequent occurrence of atrazine in surface and ground waters located in high use areas. This provides an opportunity predominantly for oral exposures to atrazine and the chlorinated metabolites via drinking water. Because atrazine’s hydroxylated metabolites dominate in plants, this provides an opportunity predominantly for oral exposures to atrazine's hydroxylated meatbolites through the transfer of residues in animal feeds to humans through the diet. Dermal exposures to atrazine, *per se,* through the transfer of residues from foliage during and after applications of atrazine products are expected because atrazine is resistant to photolysis and hydrolysis, and residues on plant surfaces are likely to be the parent compound, only. Although not expected to be a dominant exposure pathway, there is some possibility of inhalation exposures to atrazine during application.

Significant sources of exposure

As a result of the chemical's high volume of use and its tendency to persist and move with water, atrazine is one of the most frequently detected pesticides in sources of surface water (lakes, streams, and rivers) and groundwater (wells). The highest concentrations are typically seen in the Midwest region of the U.S. where the majority of the chemical is used on corn. The major source of exposure to atrazine residues is through drinking water in specified community water system (CWS) and in rural wells located in atrazine use areas. Localized seasonal pulses of atrazine residues in the months of May, June, and July in select CWS using surface water in the Midwest corn belt is the major source of exposure through the drinking water exposure pathway. These pulses occur shortly after application of atrazine in the Spring. Additional exposures through dermal contact or incidental oral exposures associated with lawn and golf course treatments may also occur. Exposures through food are minimal.

Risk assessments and populations considered

Risk assessments included in this document are: 1) an acute dietary assessment (combining a distributional analysis of one-day exposures to atrazine and the chlorinated metabolites in food with a deterministic analysis of high-end one-day exposures to atrazine and the chlorinated metabolites in drinking water); 2) a chronic dietary assessment (combining average exposures to atrazine and the chlorinated metabolites in food with a deterministic analysis of seasonal and average annual exposures to atrazine and the chlorinated metabolites in drinking water); 3) a short-term assessment based on non-occupational (residential) exposures to atrazine, *per se*, of less than 30 days; and 4) short- and intermediate-term assessments of occupational exposures to atrazine, *per se*, under various use scenarios. Atrazine's chlorinated metabolites are: desethyl atrazine, desisopropyl atrazine, and diaminochlorotriazine (DACT).

The acute dietary risk assessment aggregates exposures to residues of atrazine and the chlorinated metabolites in food and drinking water. Under the acute dietary risk assessment, "females 13 to 50 years old" is the only relevant population subgroup considered. The toxicity endpoint of concern is based on developmental effects resulting from exposure of the fetus either in utero or through lactation. The effect is attributable to a single exposure of a pregnant or lactating female. An appropriate toxicity endpoint of concern attributable to a single exposure was not identified for the general population, including infants and children. This indicates that although there is exposure, no direct acute hazard exists for these population subgroups. Rather, the developmental effect is realized only through maternal exposure.

Chronic dietary risk assessments were conducted for: i) atrazine and the chlorinated metabolites, and ii) the hydroxylated atrazine metabolites, and include all population subgroups (i.e, the general population including infants and children; a separate endpoint of concern was not identified for females of child bearing age). The chronic dietary risk assessment for atrazine and the chlorinated metabolites

aggregates combined exposures to residues of atrazine and the chlorinated metabolites in food and drinking water. Because a toxic endpoint for chronic effects of hydroxyatrazine was determined that is distinct from the toxic endpoints determined for atrazine and the chlorinated metabolites, a separate chronic dietary risk assessment for exposures to the hydroxylated metabolites of atrazine in food only was conducted and included in this assessment. The risk assessment for the hydroxy metabolites of atrazine included food as the only exposure pathway, because exposures to the hydroxy compounds are not expected to be significant in drinking water relative to exposures to atrazine and the chlorinated compounds in drinking water, and residue data on the hydroxy compounds in finished drinking water were limited.

Because short-term residential exposures to atrazine, *per se*, are anticipated based on its registered use pattern, a short-term aggregate risk assessment combining short-term (1 to 30 days) residential exposures to atrazine, *per se*, with dietary (food and drinking water) exposures to atrazine and the chlorinated metabolites was conducted. Short-term exposures for adults handling and applying atrazine products, and for adults and toddlers exposed to atrazine residues after application (post-application exposures) are included.

Intermediate-term exposures (30 days to several months) to atrazine resulting specifically from residential uses are not anticipated; therefore, an intermediate-term aggregate risk assessment inclusive of residential exposures was not conducted for atrazine. Chronic exposures (several months to lifetime) to atrazine as a result of residential uses are not anticipated; therefore, the chronic aggregate risk assessment includes only those exposure pathways relevant for chronic exposure, i.e., food and drinking water. The same toxicologic endpoint was selected for intermediate-term and chronic risk assessments. The effect on which the endpoint is based has been observed in animal studies between 30 days to 5 months time of daily exposure depending on dose. Exposures to atrazine in drinking water span the intermediate-term (30 days to several months) and chronic (several months to lifetime) exposure time frames through seasonal and annual exposures. Therefore, both of these exposure periods (seasonal and annual) have been included under a risk assessment for intermediate-term and chronic exposures in drinking water.

Separate risk assessments based on short-term (1 to 30 days) and intermediate-term (30 days to several months) occupational dermal and inhalation exposures to atrazine, *per se*, are included for handlers applying atrazine products, and for post-application exposures of harvesters. Where appropriate dermal and inhalation exposures were combined in the occupational risk assessments.

Atrazine's primary toxic effects and endpoints identified for risk assessment

In the risk assessments presented here, atrazine's chlorinated metabolites are considered to be of equivalent toxicity as atrazine, *per se*. The toxic effects attributed to the hydroxy metabolites of atrazine are considered to be independent of the effects atrazine, *per se*, and risks associated with exposure to these hydroxylated compounds have been assessed separately.

Acute Effects

Atrazine and the Chlorinated Metabolites:
The endpoints selected as the basis for acute risk assessment: delayed ossification in offspring, and prostatitis in the adult male offspring are based on three developmental studies, two conducted with rats and one conducted with rabbits, and a fourth study that examined the effects of maternal exposure to atrazine during lactation on prostate effects in male suckling offspring. Based on the results of these four studies, a weight-of-the-evidence approach was used to select the dose and effects observed after the test animals received one-day exposures to atrazine in their diets. These effects are the basis of the acute one-day reference dose (aRfD) of 0.10 mg/kg/day, which is used to assess risks associated with acute dietary exposures, short-term (1 to 30 days), incidental, oral exposures, and short-term (1 to 30 days) inhalation exposures. These effects have been identified as relevant for females 13 to 50 years old because the developmental effects on which this endpoint is based (delayed ossification in the offspring and prostatitis in the adult male) occur only through maternal exposure, i.e., in utero via a pregnant female or via lactation, rather than through direct exposure of the offspring.

Hydroxyatrazine:
A toxicological endpoint attributable to one-day exposures to hydroxyatrazine in the diet could not be identified. Therefore, a risk assessment for single exposures to hydroxyatrazine was not conducted.

Short-term Effects

The endpoint selected as the basis for short-term risk assessment: decreases in body weight gain and food consumption are based on the same three developmental studies, two conducted with rats and one conducted with rabbits, described above. This endpoint is applicable to all populations.

Intermediate-term and Chronic Effects

Atrazine and the Chlorinated Metabolites:
Atrazine alters hypothalamic gonadotrophin releasing hormone (GnRH) release in rats. There are also some data that indicate that atrazine diminishes norepinephrine in the rat hypothalamus as an initial or early site of action which in turn leads to diminished GnRH release. Atrazine also increases dopamine levels which can result in a diminished pituitary secretion of prolactin. Therefore, atrazine appears to operate at the level of the hypothalamus. In both humans and rats, hypothalamic GnRH controls pituitary hormone secretion (*e.g.*, luteinizing hormone (LH), and prolactin (PRL). The hypothalamic-pituitary axis is involved in the development of the reproductive system, and its maintenance and functioning in adulthood. Additionally, reproductive hormones modulate the function of numerous other metabolic processes (*i.e.*, bone formation, and immune, cental nervous system (CNS) and cardiovascular functions). Therefore, altered hypothalamic-pituitary function can potentially broadly

affect an individual's functional status and lead to a variety of health consequences.

The report of the Scientific Advisory Panel (SAP) convened in June 2000 to consider these health consequences of exposure to atrazine, indicated that "..it is not unreasonable to expect that atrazine might cause adverse effects on hypothalamic-pituitary function in humans." Therefore, atrazine's effect on ovarian cycling and the pre-ovulatory LH surge (as well as its effects on pregnancy, puberty, suckling induced PRL release which leads to prostatitis) are viewed as neuroendocrinopathies or biomarkers indicative of atrazine's ability to alter hypothalamic-pituitary function in general. It should be noted that atrazine's neuroendocrine effects have been demonstrated in several strains of rats (SD, Long Evans, and Wistar).

Attenuation of the luteinizing hormone (LH) surge, considered a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function, and estrous cycle disruptions demonstrated in female rats (e.g.,Sprague-Dawley and Long Evans) is the basis of the chronic reference dose (cRfD) of 0.018 mg/kg/day, and is used to assess risks associated with chronic dietary exposures, intermediate-term, and long-term oral incidental, dermal, and inhalation exposures. Alteration of the hypothalamic-pituitary function as evidenced through the attenuation of the LH surge was dose-dependent and observed between 1 to 5 months of daily dosing in a 6 month study, making this endpoint an appropriate endpoint to assess intermediate-term (30 days to several months) and chronic (several months to lifetime) exposures to atrazine. Although this specific effect (attenuation of the LH surge) is operative in females, it was selected as the basis for chronic risk assessment for all population subgroups, because it is the most sensitive endpoint available from the toxicity database and therefore protective of other adverse effects, and it is indicative of alterations of the hypothalamic/pituitary/gonadal axis, which may occur in the offspring and adults of other species (humans).

Hydroxyatrazine:
In a combined chronic/carcinogenicity study conducted with Sprague-Dawley (BR strain) rats, both male and female rats exhibited gross and histopathological effects in the kidneys after exposure to hydroxyatrazine. A chronic RfD of 0.01 mg/kg/day was derived from this endpoint for chronic dietary risk assessment.

Carcinogenic Effects

Atrazine and the Chlorinated Metabolites:
The Agency's Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP), convened in June 2000, determined that the mode of action for the carcinogenic potential in the Sprague-Dawley rat is not likely to be operative in humans. HED's Cancer Assessment Review Committee (CARC) concurred with the SAP, also concluding that the mode of action is not relevant to humans. This conclusion was based on the following considerations: though hypothalamic disruption of pituitary function (i.e., attenuation of the LH surge) and resulting estrous cycle disruption may be occurring in humans following atrazine exposure, the hormonal environment resulting from these events

would be expected to be much different from the hormonal environment seen in the rat. The prolonged/increased exposure to estrogen and prolactin as seen in the rat would not be expected to occur in humans. The prolonged/increased exposure to estrogen and prolactin in the rat is the basis of early-onset and increased mammary tumors in susceptible strains of rats. Additionally, the mutagenicity database is quite extensive and indicates that atrazine is not mutagenic. Consequently, in accordance with the *1999 Draft Guidelines for Carcinogen Risk Assessment*, the CARC classified atrazine "not likely to be carcinogenic to humans". Therefore, a cancer risk assessment was not conducted for atrazine.

Hydroxyatrazine:
No treatment-related increases in incidences of tumors of any type was observed in the treated male or female animals in the combined chronic/carcinogenicity study conducted with Sprague-Dawley (BR strain) rats. In particular, there was no increase above control levels in the incidence of mammary gland tumors in either males or females. In addition, onset times for mammary gland tumors in female rats were not decreased in this study. Therefore, a cancer risk assessment was not conducted for hydroxyatrazine.

FQPA Considerations

Atrazine and the Chlorinated Metabolites:
The FQPA Safety Factor Committee, following review of the hazard and exposure (food, water and residential) data, recommended that the FQPA safety factor for special sensitivity in infants and children be retained at 10x when assessing parent atrazine and its chlorinated metabolites (represented by diaminochlorotriazine or DACT) based on the following factors:

- Qualitative evidence of increased susceptibility, given the prostate inflammation and delay in puberty in rat studies (in males and females with atrazine and in males with DACT), which are consistent with the atrazine's neuroendocrine mode of action;

- Cause for concern for infants and children given the evidence from special studies describing the central nervous system (CNS) mode of action (specifically, neurotransmitter and neuropeptide alterations in the hypothalamus);

- Quantitative increased susceptibility was demonstrated in a prenatal developmental toxicity study with DACT in rats (developmental effects were seen in the absence of maternal toxicity);

- Uncertainty in the toxicology database resulting in the Hazard Identification Assessment Review Committee (HIARC) recommendations for studies examining specific CNS, developmental reproductive, and hormonal alterations be performed. Additionally, the HIARC required that a two-generation study be conducted with DACT employing the Office of Pollution Prevention and Toxic Substances (OPPTS) Series 870 Guidelines; and

- Some uncertainty in the water monitoring data regarding the estimation of chlorinated metabolites in groundwater.

The FQPA safety factor is being applied across all aggregate risk assessments based on estimated dietary and residential exposures for all populations considered in these risk assessments. The FQPA safety factor has not been applied to any occupational risk assessments.

As per the Office of Pesticide Program's (OPP's) policy, a reference dose (RfD) modified by an FQPA safety factor is referred to as a population-adjusted dose (PAD). As a FQPA safety factor was retained as 10X for atrazine, an acute PAD of 0.01 mg/kg/day, and a chronic PAD of 0.0018 mg/kg/day were used to estimate risk in the assessments based on acute and chronic aggregate exposures, respectively.

Hydroxyatrazine:
The FQPA Safety Factor Committee following review of the hazard and exposure (food, water and residential) data recommended that the FQPA safety factor be removed (1x) when assessing the hydroxy-metabolites since:

- There was no evidence of increased susceptibility in the prenatal developmental toxicity study in rats with hydroxyatrazine;

- There is no evidence of neurotoxicity from the submitted toxicity studies;

- The neuroendocrine effects described for atrazine are postulated to be part of a cancer mode of action for atrazine. Because hydroxyatrazine is non-carcinogenic, the current belief is that the neuroendocrine effects described for atrazine are not occurring following hydroxyatrazine exposure;

- The dietary and non-dietary exposure assessments do not underestimate the potential exposures for infants and children; and

- The drinking water exposure concerns expressed for atrazine and the chlorinated metabolites do not apply to hydroxyatrazine, given its dissimilar toxicological profile and environmental fate properties that indicate that hydroxyatrazine is less mobile in soil/water systems.

As per the Office of Pesticide Program's (OPP's) policy, a reference dose (RfD) modified by an FQPA safety factor is referred to as a population-adjusted dose (PAD). As a FQPA safety factor was reduced to 1x for hydroxyatrazine, the chronic RfD and chronic PAD are equal, and a chronic PAD of 0.01 mg/kg/day was used to estimate risk in the assessments based on chronic exposures to

hydroxyatrazine through food, only.

Preliminary risk estimates for dietary (food) exposures to atrazine

HED's Metabolism Assessment Review Committee (MARC) has determined that the residues of concern for acute dietary risk are: (i) atrazine and the chlorinated metabolites. The MARC has also determined that the residues of concern for chronic, non-cancer dietary risk are: (i) atrazine and the chlorinated metabolites, and (ii) combined free hydroxy-metabolites. Separate chronic RfDs have been identified for each of these sets of residues for the purposes of dietary exposure assessment. Therefore, acute and chronic dietary exposure and risk assessments have been conducted for the combined residues of atrazine and the chlorinated metabolites. Because the HIARC assigned a separate chronic toxicological endpoint (and chronic RfD) to hydroxyatrazine, a chronic dietary risk assessment based on food exposures, only, has been conducted for the combined residues of atrazine's four hydroxylated metabolites. All four compounds are assumed to have the same toxicological effect and their combined residues have been compared to the endpoint specific to hydroxyatrazine in a separate risk assessment. No acute toxicological endpoint was identified for hydroxyatrazine.

Risk estimates are presented in this document as percentages of the PAD. Risk estimates for acute exposures less than 100% of the acute PAD and chronic exposures less than 100% of the chronic PAD are below HED's level of concern. Risk estimates do not exceed HED's level of concern, i.e., are less than 100% of the acute PAD or chronic PAD, for either acute exposures or chronic exposures to residues of atrazine in food for any of the relevant population subgroups analyzed. Risk estimates for one-day exposures in food to combined residues of atrazine and its chlorinated metabolites are less than 1% of the acute PAD for the relevant population subgroup, females 13 to 50 years old. The risk estimates for acute dietary exposures through food are based on a probabilistic assessment using distributional data on dietary consumption and body weights with anticipated residues on foods incorporating percent of the crop-treated data. Distributions of monitoring data for food residues where available were used as appropriate. Risk estimates for long-term, average exposures in food to combined residues of atrazine and its chlorinated metabolites are less than 1% of the chronic PAD for all population subgroups analyzed. The risk estimates for chronic dietary exposures through food are based on a deterministic assessment using point estimates of average dietary consumption, average body weights, with average residues of atrazine and the chlorinated metabolites in foods, and incorporating percent of the crop-treated data.

Long-term, average exposures to the hydroxy-metabolites of atrazine in food do not exceed HED's level of concern for chronic effects for all relevant populations included in the analysis. A separate risk assessment for exposures to hydroxy-metabolites of atrazine in food indicate that all risk estimates are less than 1% of the chronic PAD for hydroxyatrazine. Estimated exposures to the hydroxy metabolites of atrazine in food, though still minimal, are marginally greater than estimated exposures to atrazine and

the chlorinated metabolites in food. This is expected as the hydroxy metabolites are the dominant plant metabolites of atrazine.

Preliminary risk estimates for drinking water exposures to atrazine

Risk estimates associated with drinking water presented here are based on exposures to combined residues of atrazine and the chlorinated metabolites. These are the residues of atrazine expected to occur in drinking water in significant quantities, and monitoring data were available for these compounds in finished drinking water. Exposure to the hydroxy metabolites of atrazine in drinking water was not included in the drinking water risk assessment, because exposure to these compounds in drinking water is expected to be significantly less than exposure to atrazine and the chlorinated metabolites, and monitoring data on the hydroxy compounds in finished drinking water were limited to residues in rural wells with targeted for high-end exposures.

Preliminary risk estimates for exposures to residues of atrazine and the chlorinated metabolites in drinking water have been provided for populations receiving their drinking water from community water systems (CWS) using surface water, and individual rural wells located in atrazine use areas. Exposure and risk estimates have been conducted for each CWS and rural well for which data on atrazine and the chlorinated metabolites were available. For CWS using groundwater, a partial assessment for atrazine, only, relative to OW's MCL of 3 ppb has been provided. OPP anticipates the submission of data allowing for an estimation of atrazine's chlorinated metabolites in CWS using groundwater, and at that time, OPP can provide preliminary risk estimates for this source of drinking water. HED has considered the available data on atrazine residues in drinking water inclusive of treatment effects, if treatment was used, i.e., HED used monitoring data for finished drinking water in these risk assessments.

<u>Risk Estimates for One-Day Exposures to Atrazine and the Chlorinated Metabolites in CWS using Surface Water</u>

Based on both a national deterministic assessment and a deterministic assessment for individuals with high-end exposures, the measured maximum one-day concentrations of atrazine plus estimates of the chlorinated metabolites in drinking water do not exceed HED's level of concern for acute effects, regardless of source, for any relevant population subgroup. Under HED's deterministic approach to estimating aggregate risk from exposures to measured residues of atrazine plus estimates of the chlorinated meatbolites in drinking water, one-day concentrations of residues of atrazine and the chlorinated metabolites less than 298 ppb do not exceed HED's level of concern for acute effects. This value (298 ppb) is the acute drinking water level of comparison (acute DWLOC) value for females 13 to 50 years old, and was calculated based on a 99.9th percentile food exposure for this subgroup of 0.000041 mg/kg/day, a 60 kg body weight, a 2L/day drinking water consumption rate, and an acute PAD of 0.01 mg/kg/day. It represents the one-day (maximum) concentration of residues of atrazine

and the chlorinated metabolites in drinking water for the relevant subgroup considered under the acute risk assessment that is not expected to result in adverse acute health effects after considering one-day exposures to residues of atrazine and the chlorinated metabolites in food at the 99.9th percentile of exposure. Based on a variety of databases containing drinking water residue data for atrazine, the maximum measured concentration of atrazine plus an estimation of the chlorinated metabolites in any CWS monitoring for atrazine under the SDWA from 1993 to 1998, was 89 ppb. The maximum measured concentration of atrazine plus the chlorinated metabolites in the rural drinking water wells in atrazine use areas monitored by the registrant was 18 ppb.

Risk Estimates for Intermediate- term (seasonal) and Chronic (annual) Exposures to Atrazine and the Chlorinated Metabolites in CWS using Surface Water

Under HED's deterministic approach to estimating aggregate risk for atrazine in drinking water, seasonal mean and annual average concentrations of residues of atrazine and the chlorinated metabolites less than 12.5 ppb do not exceed HED's level of concern for chronic effects. This value (12.5 ppb) is the chronic DWLOC value for infants (< 1 year old), and was calculated based on an average food exposure for this subgroup of 0.000008 mg/kg/day, a 7 kg body weight, a 1L/day drinking water consumption rate, and a chronic PAD of 0.0018 mg/kg/day. Chronic DWLOC values used in this assessment ranged from 12.5 ppb for infants less than 1 year old weighing 7 kg to 68 ppb for adult males weighing 76 kg. Chronic DWLOC values represent the average daily concentration of atrazine and the chlorinated metabolites in drinking water that is not expected to result in adverse chronic health effects after considering long-term, average exposures to residues of atrazine and the chlorinated metabolites in food for each population subgroup of interest. The maximum measured seasonal mean and annual average concentrations of atrazine plus estimations of the chlorinated metabolites in any surface water-sourced CWS monitoring for atrazine under the SDWA from 1993 to 1998, were 61.6 ppb (seasonal) and 18.9 ppb (annual), repsectively.

Based on both a national deterministic assessment and a deterministic assessment for individuals with high-end exposures, measured annual average concentrations of residues of atrazine plus estimations of the chlorinated metabolites in drinking water from CWS using surface water do not exceed HED's level of concern for chronic effects for any adult (male and female) population subgroup. One CWS had seasonal mean concentrations of approximately 62 ppb in 1993 exceeding a chronic DWLOC value for adult females of 54 ppb. This is the maximum seasonal mean concentration measured at any CWS in the available databases. Risk estimates for this CWS in Salem, IL exceeded HED's level of concern for adult females as well as infants and children (with a chronic DWLOC value of 12.5 ppb) in 1993, only, and not in any subsequent years for which monitoring data were available. All other CWS during the period of monitoring from 1993 to 1998, had seasonal mean concentrations at levels that did not exceed HED's level of concern for any adult (male and female) population subgroup.

Under the deterministic exposure assessment for drinking water, seasonal mean and/or annual average concentrations of atrazine plus its chlorinated metabolites exceeded HED's level of concern for infants

and/or children's subgroups in up to 24 CWS using surface water. These 24 CWS are: Gillespie, Hettick, Shipman, Salem, Palmyra-Modesto, Hillsboro, Farina, Kinmundy, ADGPTV, Carlinville, West Salem, Flora, Sorento, Whitehall, Centralia, and Wayne City in Illinois, Chariton in Iowa, Batesville, Holland, North Vernon, and Scottsburg in Indiana, Iberville in Louisiana, and Bucklin, and Vandalia in Missouri. The CWS at Gillespie, Palmyra-Modesto, Hillsboro, and ADGPTV sell drinking water to purchasers, thus, these 24 CWS are believed to serve approximately 130,000 people. The U.S. Census Bureau estimates that children under 5 years old represent 6.87% of the U.S. population. Thus, approximately 9000 children potentially have exposure to residues of atrazine and the chlorinated metabolites in their drinking water at levels that exceed concern.

HED notes that the Shipman reservoir (serving approximately 650 people) no longer serves as a drinking water source; in 1999 the town of Shipman was switched to an alternative source of drinking water. The drinking water source at Whitehall was switched from surface water to groundwater in 1997.

These 24 CWS are monitored under the SDWA for atrazine. These 24 CWS represent variously 0.11% of all CWS monitoring for atrazine under the SDWA using either surface or groundwater or a blend, 0.5% of the 4886 CWS using surface water, and 0.65% of the 3670 CWS using surface water with data on atrazine residues. Under this deterministic assessment, these 24 CWS have been identified for probabilistic risk assessment. Probabilistic assessments using all available distributional data on drinking water residues, body weights, and drinking water consumption would reduce the uncertainty associated with these risk estimates, which have been calculated deterministically.

Risk Estimates for One-Day and Chronic Exposures to Atrazine and the Chlorinated Metabolites in Domestic Rural Wells used for Drinking Water

Approximately 10% of the U.S. population receives their drinking water from rural wells, cisterns or springs, which are not regulated under the SDWA. Acute (one-day) exposures to atrazine and the chlorinated metabolites in drinking water from rural wells do not exceed HED's level of concern. Chronic exposures of adult populations using rural wells for drinking water do not exceed HED's level of concern. HED has some concerns for chronic exposures of the subpopulation of infants and children getting their drinking water from rural wells located directly in atrazine use areas, i.e., adjacent to fields where atrazine was used. Eight wells out of 1505 wells selected based on their location in areas with high atrazine use were tested and had residues of atrazine and the chlorinated metabolites approaching, equal to, or greater than 12.5 ppb. As this risk estimate is based on only one sample per well, additional sampling at these wells would reduce HED's uncertainty regarding average concentrations of atrazine residues in these wells.

Risk Estimates for Exposures in CWS using Groundwater

The registrant provided a partial assessment (contained in Attachment VII) using the available

compliance monitoring data collected under the SDWA on residues of atrazine, *per se*, in finished drinking water from CWS using groundwater. Data to estimate concentrations of the chlorinated metabolites in CWS using groundwater are still being developed, and were not available at this time. Because estimations of the chlorinated metabolites for these CWS could not be made at this time, a comparison to acute and chronic DWLOC values has been reserved until these estimations can be made. However, for the portion of the U.S. population receiving their drinking water from CWS using groundwater as the source (73,856,519 people), HED notes that approximately 4% of the CWS using groundwater and 3.33% of the population served by CWS using groundwater had detections of atrazine residues in finished drinking water, whereas, 42% of CWS using surface water and 33.5% of the population served by CWS using surface water had detections of atrazine residues in finished drinking water. Although the risk assessment is incomplete without an estimate of the chlorinated metabolites in each CWS using groundwater, the preliminary indication is that CWS using groundwater are not impacted nearly as heavily by atrazine use as CWS using surface water. However, HED reserves its preliminary risk estimate for CWS using groundwater until the data for estimating concentrations of the chlorinated metabolites in CWS using groundwater are available, and the risk assessment for CWS using groundwater can be completed.

Additional Concerns

There are some CWS using surface water with maximum measured concentrations of atrazine and estimations of the chlorinated metabolites approaching, equal to, or greater than chronic DWLOC values for infants and children's groups, but with annual average concentrations below chronic DWLOC values that were not included in the more intensive sampling programs sponsored by industry. There are no seasonal mean concentrations for these CWS to compare to chronic DWLOC values, only maximum and annual average concentrations. These CWS may have seasonal mean concentrations either above or below chronic DWLOC values. Although a direct comparison of these maximum measured concentrations to chronic DWLOC values would be inappropriate, this finding introduces a source of uncertainty into this risk assessment as it cannot be known from the available data if these CWS have seasonal mean concentrations of atrazine residues above chronic DWLOC values, and therefore, have risk estimates above HED's level of concern. Some of these CWS are listed in Appendix E for the OW's use in consideration of any necessary actions for these CWS. OW may want to consider including these CWS under any future seasonal compliance monitoring schemes. The list in Appendix E may not necessarily be complete.

Preliminary risk estimates associated with residential exposures to atrazine

Risk estimates for residential exposures to atrazine consider exposure to atrazine, *per se*, because only the parent compound is expected to be available for exposure on the surfaces of the foliage treated, and monitoring data were collected for the parent compound only. Residues of the chlorinated and hydroxylated metabolites are not expected on plant surfaces. Dermal, dietary (food and drinking water), and inhalation exposures have been combined as appropriate for adults. Dermal, dietary (food

and drinking water), and incidental oral exposures have been combined as appropriate for children.

Risk estimates for residential exposures to atrazine are expressed as Margins of Exposure (MOEs). Residential exposure scenarios with MOEs greater than 1000 do not exceed HED's level of concern. Risk estimates for combined short-term (1 to 30 days) residential dermal and inhalation exposures for adult handlers applying atrazine to lawns, estimated using HED's Standard Operating Procedures for Estimating Residential Exposures (Residential SOPs) and available Occupational and Residential Exposure Task Force (ORETF) data, do not exceed HED's level of concern; i.e., all MOEs for all exposure scenarios are greater than 1000. Intermediate-term exposures, greater than 30 days in duration, are not expected to result from adult handlers applying atrazine to lawns; therefore, risk assessments for intermediate-term residential exposures for adult handlers were not conducted.

Short-term residential post application exposure estimates exceed HED's level of concern for adults and toddlers exposed dermally while playing on lawns immediately after treatment with atrazine. MOEs for children and adults playing on turf one day after treatment are estimated to be 390 and 660, respectively. After the 2nd day, MOEs are above 1000 for both children and adults under this exposure scenario. Risk estimates for toddlers' short-term exposures to atrazine through incidental oral exposures also exceed HED's level of concern. The risk estimate (MOE) for children mouthing their fingers after contact with treated grass was 330, while mouthing grass and soil ingestion had MOEs of 1800 and 100,000, respectively. The aggregation of all of these mouthing activities (mouthing fingers + mouthing grass + soil ingestion) results in a MOE of 280. MOEs for incidental oral exposures for toddlers range from 25 to 180 for granule ingestion exposure scenarios. Combined dermal and incidental oral exposures of toddlers exceed levels of concern. Intermediate-term post application residential exposures, greater than 30 days in duration, are not expected as a result of residential uses of atrazine; therefore, risk assessments for intermediate-term post application residential exposures were not conducted.

Preliminary risk estimates associated with occupational exposures to atrazine

Risk estimates for occupational exposures to atrazine consider exposure to atrazine, *per se*, because only the parent compound is expected to be available for exposure on the surfaces of the foliage treated, and monitoring data were collected for the parent compound only. Residues of the chlorinated and hydroxylated metabolites are not expected on plant surfaces.

For short-term exposure estimates based on either PHED data, chemical specific exposure studies, and/or ORETF data, with appropriate personal protective equipment (PPE) or engineering controls, all short-term aggregate (dermal and inhalation) handler exposure scenarios had MOEs greater than 100, and thus, do not exceed HED's level of concern. There were no exposure data for liquid/liquid fertilizer treatment, so risk estimates for this scenario could not be calculated. Based solely on PHED data, and after consideration of personal protective equipment (PPE) or engineering controls, all short-term aggregate (dermal and inhalation) exposure scenarios had MOEs greater than 100. Engineering

control methods were only required to mitigate exposure for one scenario. Using the ORETF study data, where applicable, baseline short-term MOEs for lawn care operators (LCOs) spraying lawns or applying granular formulations were all greater than 100. Where PHED data were used, all LCO scenarios had MOEs greater than 100 with the use of gloves.

For intermediate-term exposure estimates based on either PHED data, chemical specific exposure studies, or a combination of these data, with appropriate personal protective equipment (PPE) or engineering controls, most (approximately 80%) intermediate-term aggregate (dermal and inhalation) handler exposure scenarios had MOEs greater than 100, and thus, do not exceed HED's level of concern. There were no exposure data for liquid/liquid fertilizer treatment, so risk estimates for this scenario could not be calculated. Using PHED data incorporating PPE and/or engineering controls, 109 of the 139 (78%) of the handler exposure scenarios had intermediate-term aggregate (dermal and inhalation) MOEs greater than 100. There were no data for liquid/liquid fertilizer treatment and the right-of-way and hand sprays had no known engineering controls. Using the ORETF study data, all baseline clothing intermediate-term LCO handler scenarios had MOEs greater than 100. Where PHED data was used, LCO handlers required additional PPE to achieve MOEs greater than 100.

Intermediate-term exposures that exceed HED's level of concern are generally associated with mixing and loading of the largest quantities (liquid or dry flowable/WDG) of atrazine. Examples include the higher application rates and acerages for use on chemical fallow lands, grasslands, corn, sorghum, and in fertilizer admixture. With engineering controls, all applicator risk estimates have MOEs above 100.

For all scenarios considered, post application short-term and intermediate-term dermal exposures to atrazine resulted in risk estimates that do not exceed HED's level of concern.
Appropriate protective clothing to protect the skin and eyes of handlers and field workers is recommended. For workers who may have extensive exposure to atrazine, skin protection should be required. Based on the estimated risks, all occupational handlers of atrazine should wear chemical resistant gloves, and enclosed systems should be used when handling large quantities. These risk estimates and recommendations are supported by the analysis of the incident data.

Preliminary aggregate risk estimates for acute, short-term, and intermediate-term to chronic exposures to atrazine through the diet, drinking water, and residential use

The aggregate risk assessments presented in this document estimate risks associated with combined exposures to atrazine residues through multiple exposure pathways, specifically, through combining residues of atrazine and the chlorinated metabolites in food and drinking water (dietary), with residues of atrazine, *per se*, from home uses. As previously stated, residues of atrazine and the chlorinated metabolites are considered toxicologically equivalent and are expected to occur in food and drinking water, and exposures to residues of atrazine, *per se*, are expected on grasses from residential uses. Exposure to atrazine's chlorinated metabolites is not expected to occur from contact with plant surfaces. Under HED's approach to incorporating drinking water exposures into estimates of aggregate

risk, an exposure scenario exceeds HED's level of concern when measured concentrations of atrazine and the chlorinated metabolites are greater than the DWLOC values calculated for specific population subgroups.

Exposures to hydroxyatrazine were considered for the food exposure pathway, only, and were not aggregated with exposures through any other pathway for the following reasons: 1) residues of hydroxyatrazine are expected to form in the most significant quantities once absorbed and metabolized in plant tissues; 2) residues are not expected to form on plant surfaces; 3) residues are formed to a lesser extent than the chlorinated metabolites in water; and 4) monitoring data on these compounds in finished drinking water were limited.

Acute Aggregate Risk Estimates

The aggregate risk assessment for acute exposures to atrazine and the chlorinated metabolites combines high-end, one-day exposures through food and drinking water, only. Exposure to atrazine from food sources (based on 99.9th percentile exposure estimates) and drinking water (based on surface and ground water monitoring data on finished drinking water) do not exceed HED's level of concern for acute dietary risk for the relevant subgroup, females 13 to 50 years old.

Aggregate Risk Estimates Acute (one-day) Exposures to Combined Residues of Atrazine and the Chlorinated Metabolites		
Exposure Pathway	Population Assessed	Risk Estimates
Food	Females 13 to 50 years old	< 1% acute PAD
Food + Drinking water	Females 13 to 50 years old	Maximum measured concentrations of atrazine residues in drinking water (89 ppb) are below acute DWLOC value (298 ppb) in all CWS assessed

Intermediate-term and Chronic Aggregate Risk Estimates

The aggregate risk assessment for intermediate-term and chronic exposures to atrazine and the chlorinated metabolites combines estimates of high-end seasonal (intermediate-term) or annual average (chronic) exposures to atrazine through drinking water with long-term average exposures through food. Intermediate-term (30 days to several months) and chronic (several months to lifetime) exposures are not expected to occur from residential uses of atrazine. Therefore, aggregate risk assessments inclusive of intermediate-term and chronic residential exposures were not conducted, and the intermediate-term and chronic aggregate risk estimates are the same as those summarized above for intermediate-term and chronic drinking water risks. Up to 24 CWS using surface water have risk estimates for intermediate-term and chronic exposures (based on seasonal mean concentrations of residues of atrazine and the chlorinated metabolites) exceeding HED's level of concern for infants. These 24 CWS have been identified for probabilistic risk assessment using all available distributions of data on atrazine residues in drinking water, food consumption, and body weights.

In addition, eight rural wells out of 1505 tested have concentrations of atrazine and the chlorinated metabolites above HED's level of concern for infants. Exposures from these wells represent high-end exposures for individuals living in rural areas and in close proximity to areas where atrazine use is high. These wells do not represent a national exposure for all individuals using rural wells for drinking water.

Aggregate Risk Estimates for Intermediate-term (seasonal) and Chronic (annual) Exposures to Combined Residues of Atrazine and the Chlorinated Metabolites		
Exposure Pathway	Population Assessed	Risk Estimates
Food	Adults (males)	< 1% chronic PAD
	Adult (females)	< 1% chronic PAD
	Infants and children	< 1% chronic PAD
Food + Drinking Water	Adults (males)	Measured seasonal (~62 ppb) and annual average (~20 ppb) atrazine residue concentrations are below chronic DWLOC values in all CWS assessed in all years
	Adult (females)	Maximum measured seasonal average atrazine residue concentration (~62 ppb) was greater than chronic DWLOC value (54 ppb for adult females) in one CWS in 1993 only
	Infants and children	Measured seasonal average atrazine residue concentrations (11 ppb to ~20 ppb) were approaching, equal to, or greater than chronic DWLOC value (12.5 ppb) for infants < 1 year old) in 24 CWSin at least one year

Short-term Aggregate Risk Estimates

For those regions of the U.S. where atrazine is used at home (the Southeast), short-term aggregate risk estimates exceed HED's level of concern for adults and toddlers coming into contact with turf either during application or within one week after application. Because several of the residential short-term exposure scenarios for adults and children have risk estimates exceeding HED's level of concern based on either dermal and/or incidental oral exposures, alone, combining these exposures with additional dietary exposures (via food and drinking water) would result in risk estimates further exceeding HED's level of concern.

Aggregate Risk Estimates for Short-term (1 to 30 days) Exposures		
Exposure Pathway	Population Assessed	Risk Estimates
Food + Drinking Water + Residential	Adults (males and females) applying atrazine	Measured maximum, weekly, seasonal and annual average concentrations of atrazine residues in drinking water are less than short-term DWLOC values based on combined exposures from food, drinking water, and dermal pathways
	Adults (males and females) post application	Measured maximum, weekly, seasonal and annual average concentrations of atrazine residues in drinking water are greater than short-term DWLOC values based on combined exposures from food, drinking water and dermal pathways for one exposure pathway
	Toddlers post application	Measured maximum, weekly, seasonal and annual average concentrations of atrazine residues in drinking water are greater than short-term DWLOC values based on combined exposures from food, drinking water, dermal and incidental oral pathways

Uncertainties and levels of confidence associated with these preliminary risk estimates

All risks assessments presented in this document were conducted using deterministic approaches, with the exception of the acute dietary risk assessment. As such, all preliminary risk estimates presented in this document are considered to be conservative. Major sources of uncertainty associated with each risk assessment are mentioned here, but all relevant sources of uncertainty are discussed under each specific risk assessment in detail.

Risk Estimates for Food Exposures

HED believes the risk estimates for acute and chronic exposures to residues of atrazine through food are conservative. The confidence associated with these risk estimates is high. The data available for dietary exposure assessment were of very high quality being either USDA's monitoring data or residue data from adequate field trials and plant and animal metabolism studies. All available monitoring, field trial, and metabolism study data on atrazine residues in plant and animal commodities were used to estimate anticipated residues for the majority of human food items included in the dietary assessments. Tolerance level residues representing the maximum residue expected to occur from labeled uses of atrazine were used for guava only. The best available information on the percentage of crop treated was also included. The acute dietary assessment used probabilistic techniques to estimate exposure.

Risk Estimates for Drinking Water and Food Exposures

HED believes the risk estimates are conservative for the portion of the population receiving their drinking water from CWS using surface water. The confidence associated with these risk estimates is high. The data available for drinking water exposure assessment were extensive and of very high quality. The most recent changes to atrazine use rates should be reflected in these data. These exposures and risks have been estimated using a deterministic approach, in which, a single residue value, either a maximum value for acute effects or a seasonal or annual average value for intermediate-term and chronic effects, is assumed along with default drinking water consumption rates and body weights for each population subgroup considered in the assessment. As this risk assessment for drinking water exposures to residues of atrazine and the chlorinated metabolites is based on a deterministic methodology, a probabilistic assessment using all available data on atrazine residues in drinking water, consumption, and body weights in a distributional analysis would provide more accurate estimates of risk.

HED further believes these risk estimates based on seasonal pulses of residues of atrazine and the chlorinated metabolites to be conservative because atrazine suppression of the LH surge is time and dose dependent; lower doses of atrazine require longer periods of time to produce an attenuation of the LH surge in the rat. The maximum seasonal mean concentrations were used to represent a 3-month average exposure period during May, June and July, and the relevant intermediate-term and chronic effect (attenuation of the LH surge, considered a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function) is seen in the test animals after 1 month of daily exposure at 40 mg/kg/day (lowest observed adverse effect level from Morseth 1996a) and after 4 to 5 months of daily exposure at 3.65 mg/kg/day (lowest observed adverse effect level from Morseth 1996b).

The 36 CWS identified in Appendix E introduce a source of uncertainty into the risk assessment for CWS using surface water as discussed above under the estimates of risk for exposures through drinking water. It cannot be known from the available data whether these CWS have seasonal average concentrations above a level of concern; however, there could be additional CWS that have seasonal mean concentrations of atrazine and the chlorinated metabolites that exceed HED's level of concern.

The estimates of risk for that portion of the population receiving their drinking water from rural wells in close proximity to atrazine use areas is conservative, and unrefined. HED associates a moderate level of confidence with these estimates of risk. The wells selected for monitoring were chosen because of their location in atrazine use areas, and as such they represent a set of wells with potential high-end exposures rather than a set of wells representing the national exposure. Further, only one sample was taken per well, and it cannot be known whether this one sample represents a maximum, a minimum, or some sort of average concentration value for atrazine residues in those wells. This is a major source of uncertainty for the risk assessments conducted for rural wells.

Risk Estimates for Residential Exposures

Estimates of risk associated with residential use of atrazine products are based on average high-end

residues, and standard operating procedures and assumptions that are considered to be conservative, screening-level assessments. The data available for residential exposure assessments were of high quality. HED associates a fairly high level of confidence with risk estimates for dermal post-application exposures to atrazine; however, these risk estimates resulting in MOEs which exceed the Agency's level of concern are based on the highest reported residue levels from exposure studies, and are considered conservative. Toddler's incidental oral and granular ingestion exposure scenarios are based on standard assumptions and formulae (Residential SOPs, 1999) which are designed to provide screening-level estimates of exposure. HED's confidence in the risk estimates for these exposure scenarios is low to moderate. A probabilistic approach to the use of the various residue study data would help to refine the risk estimates.

Risk Estimates for Occupational Exposures

HED has a high confidence level in the occupational risk estimates. While uncertainty cannot be completely removed from any pesticide risk assessment, there is a substantial amount of actual field monitoring data for assessing the occupational exposures of handlers of atrazine in the largest area of use, field and row crops. Available studies support the handler exposure and risk estimates stated here, given that most of the estimates are for typical-to-high application rates and acres-treated per day. Less data were available for most of the other crops and the fertilizer admixture scenarios assessed. A high level of confidence is associated with the risk estimates for post-application exposures from field crops and turf as they are based on acceptable guideline field residue study data. Most of the remaining occupational post-application risk estimates were extrapolated from those residue studies using the best available crop-specific transfer coefficients, and consequently, are considered more uncertain because of the translation of residue data from one crop to another.

Data gaps

The available database is complete and of high quality and supports this revised preliminary human health risk assessment. With the exception of a limited field rotational crop study, there are no significant data gaps for residue and product chemistry, toxicology, dietary exposure assessment (inclusive of drinking water), and occupational and residential exposures. Additional data to refine and clarify the risk estimates presented in this document include: a 870.3800 Reproduction and Fertility Effects study conducted with the atrazine metabolite diaminochlorotriazine (DACT - a mammalian metabolite of both atrazine and simazine); a limited rotational crop study; confirmatory storage stability data; an analytical method for determining atrazine's hydroxy metabolites in plants; residue data on atrazine's chlorinated metabolites in CWS using groundwater; additional sampling in rural wells; additional exposure and use data for mixing, loading, and application of dry and liquid fertilizers, both commercially (including cooperatives) and on-farm; and although not a data gap, probabilistic exposure assessments for those CWS and residential exposure scenarios with risk estimates identified in this document as exceeding HED's level of concern would help to refine these risk estimates.

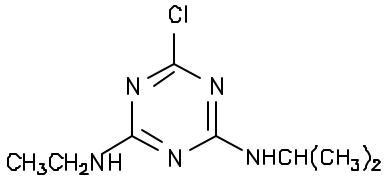
2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

Atrazine (2-chloro-4-ethylamino-6-isopropylamino-*s*-triazine) is a triazine herbicide. It is a systemic pesticide. There are no known isomeric forms or impurities of toxicological concern associated with this compound. Atrazine's chemical structure is provided below in Figure 1.

Figure 1. Chemical name and structure of atrazine

Atrazine

2-chloro-4-ethylamino-6-isopropylamino-*s*-triazine



(G-30027)

Residues of atrazine are absorbed through the plant root system, and translocated throughout the plant. Atrazine residues are not expected to be removed through simple washing and peeling. However, foliar applications of atrazine appear not to be translocated from leaves to other parts of the plant. Atrazine acts by blocking photosynthesis in plants.

In general, atrazine is moderately persistent and mobile in the environment. Atrazine resists abiotic (chemical) hydrolysis; it is stable at ambient pH, and resists aqueous photolysis. It is only moderately susceptible to degradation in soil with half-lives of 3 to 4 months in the laboratory under aerobic conditions. In anaerobic conditions, atrazine's half-life may be much longer with the water and sediment half-lives being 578, and 330 days, respectively. It is unlikely that atrazine degrades rapidly in soil, on plant foliage, or in water. Atrazine has a relatively low vapor pressure, and is not expected to volatilize rapidly from soil, foliage, or water. Atrazine is not strongly adsorbed to soil particles and organic matter; it partitions preferably into water, which may result in some volatilization from foliage. In addition, its relatively low adsorption characteristics indicate that atrazine may undergo substantial wash off from foliage. It should also be noted that foliar dissipation rates for numerous pesticides have generally been somewhat greater than otherwise indicated by their physical/chemical, and other fate properties.

These generalized physical/chemical properties affect the fate and transport of the compound and its availability in the environment in edible portions of plants, in water used for drinking, and on treated foliage. It is generally accepted that atrazine's relative persistence and mobility in the environment coupled with its widespread use on animal feed crops (corn) result in the frequent occurrence of atrazine in surface and ground waters located in high use areas. This provides an opportunity predominantly for oral exposures to atrazine and the chlorinated metabolites via drinking water and through the transfer of residues in animal feeds to humans through the diet. Dermal exposures may be expected through the transfer of residues from foliage during and after applications of atrazine products.

Although not expected to be a dominant exposure route, there is some possibility of inhalation exposures during application.

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

The toxicology database is extensive and there is a high degree of confidence in the scientific quality of the toxicity studies conducted with atrazine. Toxicity studies required under the Subdivision F Guidelines have been submitted and found acceptable by the Agency. Special studies examining the toxicology of atrazine have been performed by the registrant in addition to the required guideline studies. Additionally, EPA's National Health and Environmental Effects Laboratories (NHEERL) have performed studies investigating atrazine's neuroendocrine mode of action and related reproductive and developmental effects. These studies have been published in the peer reviewed literature. These numerous studies, taken together, define what is known to date about the toxicology associated with atrazine exposure.

Registrant-submitted studies demonstrating the endpoint selected for use in the intermediate-term and chronic risk assessments (attenuation of the luteinizing hormone (LH) surge and estrous cycle data) have been published in the open literature as well as being submitted to the EPA. There are not just one, but multiple registrant-submitted studies in which LH surge and estrous cycles are shown to be altered following atrazine exposure (four studies have been submitted demonstrating LH surge alterations and five studies have been submitted examining estrous cycle alterations). Finally, EPA's NHEERL research, which has been performed independently of the registrant-submitted data and published, demonstrate reproductive and developmental effects consistent with neuroendocrine alterations.

A summary table of each of the toxicity studies with the No Observable Adverse Effect Level (NOAEL), the Lowest Observable Adverse Effect Level (LOAEL), and the MRID numbers are presented in Appendix A. The data base for acute toxicity is complete and data on the technical product is tabulated below in Table 1:

Table 1: Acute Toxicity Data of Technical Atrazine

Guideline No.	Test	Results	Toxic Category
81-1	Oral LD_{50} - rat	LD_{50} > 1,869 mg/kg (M&F combined)	III
81-2	Dermal LD_{50} - rat	LD_{50} > 2,000 mg/kg (M&F combined)	III
81-3	Inhalation LC_{50} - rat	LC_{50} > 5.8 mg/L (M&F combined)	IV
81-4	Eye Irritation - rabbit	Non irritant	IV

Table 1: Acute Toxicity Data of Technical Atrazine			
Guideline No.	**Test**	**Results**	**Toxic Category**
81-5	Dermal Irritation - rabbit	Non irritant	IV
81-6	Dermal Sensitization	Non-sensitizer	---

Atrazine alters the release of hypothalamic gonadotrophin releasing hormone (GnRH) in rats. There are also some data that indicate that atrazine diminishes norepinephrine in the rat hypothalamus as an initial or early site of action which in turn leads to diminished GnRH release. Atrazine also increases dopamine levels which can result in a diminished pituitary secretion of prolactin. Therefore, atrazine appears to operate at the level of the hypothalamus. In both humans and rats, hypothalamic GnRH controls pituitary hormone secretion (*e.g.*, luteinizing hormone (LH), prolactin). The hypothalamic-pituitary axis is involved in the development of the reproductive system, and its maintenance and functioning in adulthood. Additionally, reproductive hormones modulate the function of numerous other metabolic processes (*i.e.*, bone formation, and immune, cental nervous system (CNS) and cardiovascular functions). Therefore, altered hypothalamic-pituitary function can potentially broadly affect an individual's functional status and lead to a variety of health consequences.

The Scientific Advisory Panel convened in June 2000 to consider the health consequences of exposure to atrazine, indicated in their report that "..it is not unreasonable to expect that atrazine might cause adverse effects on hypothalamic-pituitary function in humans." Therefore, atrazine's effect on ovarian cycling and the pre-ovulatory LH surge (as well as its effects on pregnancy, puberty, suckling induced PRL release which leads to prostatitis) are viewed as neuroendocrinopathies or biomarkers indicative of atrazine's ability to alter hypothalamic-pituitary function in general. It should be noted that atrazine's neuroendocrine effects have been demonstrated in several strains of rats (SD, Long Evans, Wistar).

A primary toxicologically significant effect is an attenuation of the proestrous afternoon luteinizing hormone (LH) surge which results in estrous cycle alterations and subsequent alterations in hormone levels. The no observed adverse effect level (NOAEL) for this effect was selected by the Hazard Identification Assessment Review Committee (HIARC) as the endpoint for risk assessments which incorporate chronic dietary exposure, and intermediate- and long-term dermal and/or inhalation exposures. This effect occurred consistently in assays conducted in the Sprague-Dawley strain of rat. The LH and estrous cycle effects have also been demonstrated in Long Evans rats, but did not occur in chronic studies conducted with the Fischer-344 strain of rat. The NOAEL of 1.8 mg/kg/day for the attenuation of LH surge was selected as the basis for establishing the chronic Reference Dose (or cRfD).

A dose-response relationship has been demonstrated for the attenuation of the LH surge in several special studies conducted by the registrant. This effect occurs in both sub chronic (6 month) and

chronic (1 to 2 year) studies. As would be expected where a causal dose-response relationship has been established, lower doses over a longer period of time are required to induce the same effects in long-term (chronic) studies compared to shorter term studies. Daily dosing at the lowest observed adverse effect level (LOAEL) of 3.65 mg/kg/day is necessary over a period of 4 to 5 months to elicit attenuation of the LH surge. Daily doses at higher levels elicit the response more quickly; attenuation of the LH surge was noted after 3 months of daily doses at 29 mg/kg/day, and after 1 month at daily doses of 40 mg/kg/day. Attenuation of the LH surge occurs normally in the Sprague-Dawley rat at 9 months of age through the normal aging process in this strain of rat.

The attenuation of the LH surge is an integral part of the neuroendocrine mode of action pathway leading to the potential carcinogenicity in the Sprague-Dawley strain of rats. The neuroendocrine effects of atrazine (i.e., alterations in GnRH, dopamine, prolactin and LH) have also been shown to play a role in certain reproductive and developmental effects in rats. This mode of action identified for cancer-associated effects in the Sprague-Dawley (SD) rat are specific to rats whose mode of reproductive senescence is "constant estrous". These effects did not occur in F-344 strain of rat, and thus only appear to occur in the SD, Long-Evans or Wistar strains.

The attenuation of the LH surge and estrous cycle disruptions appears to be a species, strain and sex specific effect occurring in female Sprague-Dawley rats, and in some other rat strains with a similar reproductive aging pattern. The Agency's FIFRA Scientific Advisory Panel (SAP) convened in June 2000 determined that the mode of action for cancer-associated effects in the Sprague-Dawley rat is not likely to be operative in humans. HED's Cancer Assessment Review Committee (CARC) concluded that the mode of action is not relevant to humans. Although hypothalamic disruption of pituitary function (i.e., attenuation of the LH surge) and resulting estrous cycle disruption may be occurring in humans following atrazine exposure, the hormonal environment resulting from these events would be expected to be much different from the environment seen in the rat. The prolonged/increased exposure to estrogen and prolactin seen in the rat would not be expected to occur in humans. Consequently, in accordance with the 1999 Draft Guidelines for Carcinogen Risk Assessment, the CARC classified atrazine as “not likely to be carcinogenic to humans”. Therefore, a cancer risk assessment was not conducted for atrazine.

There was no evidence of increased sensitivity/susceptibility demonstrated in the standard developmental and the two generation reproduction studies submitted under the Subdivision F Guideline requirements. In the two prenatal developmental toxicity studies in rats, developmental effects (delayed or (no) ossification at several sites) were seen in the presence of maternal toxicity. In the prenatal developmental toxicity study in rabbits, developmental effects (increased resorptions and delayed ossification) were seen in the presence of maternal toxicity. In the two generation reproduction study in rats, no offspring toxicity was seen in females; male offspring exhibited decreased body weight, which was seen in the presence of parental toxicity. It should be noted that the 2-generation reproductive study conducted on atrazine was a pre-1998 guideline study, which would not include sensitive measures of endocrine disruption.

Published peer reviewed studies performed by EPA's NHEERL laboratories demonstrated increased sensitivity following exposure to atrazine. Specifically, exposure of a lactating dam to atrazine during the days shortly after parturition results in an increased incidence and severity of prostate inflammation in nursing male offspring at doses in which the exposed mother displays no apparent toxic effects. Other studies by NHEERL show that exposure of developing male and female rats to atrazine delays the onset of puberty.

There is evidence that atrazine is associated with endocrine disruption. Direct measurements of norepinephrine, dopamine, and GnRH, and of serum hormones such as certain steroid hormones and luteinizing hormone, as well as changes in estrous cycling and histomorphic changes in hormone responsive tissues, indicate neuroendocrine disruption.

The Agency is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

Several assays which are classified as "Tier I Screens" under proposed EDSTAC guidelines (U.S. EPA Endocrine Disruptor Screening Program. Federal Register: August 11, 1998. 63, 154: 42852-42855) have already been performed on atrazine. These assays are described in the attached Toxicology RED chapter were primarily negative in regards to atrazine's ability to bind directly to the estrogen receptor. Other studies have also either been submitted by the Registrant, or published by EPA's NHEERL group. Unlike the "Tier I Screens" mentioned above, these studies did demonstrate an ability of atrazine to disrupt neuroendocrine activities (evidence of neurotransmitter and neuropeptide, and hormonal alterations were seen following atrazine exposure).

It should be noted that all these studies were *in vivo* studies which employed either the SD, Wistar or Long-Evans strain of rat. Registrant-submitted studies examining hormonal alterations in the F-344 rat are also available and were negative for endocrine-disrupting activity. When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, atrazine may be subjected to additional screening and/or testing to better characterize effects related to neuroendocrine disruption.

Chlorinated Metabolites:
A limited toxicology database is available for the chlorinated metabolites of atrazine. With the exception of the diaminochlorotriazine metabolite (DACT) the chlorinated metabolites appear to be of similar toxicity compared to the parent. In the prenatal developmental toxicity study in rats, there was evidence (quantitative) for increased susceptibility following exposure to DACT. The maternal LOAEL was 75 mg/kg/day and the NOAEL was 25 mg/kg/day compared to the developmental LOAEL of 25 and the NOAEL of 2.5 mg/kg/day. Developmental effects (delayed ossification of certain bones) were seen in the absence of maternal toxicity. To address this concern, the HIARC has recommended a 2-generation reproduction study with DACT.

Hydroxyatrazine:
A limited toxicology database for hydroxyatrazine compounds is available. For acute toxicity hydroxyatrazine appears to be less toxic than atrazine. The only effects seen in any of the submitted studies which may be attributable to a single dose were developmental alterations in the developmental rat study. The developmental alterations seen in this study were seen only at the high dose, were few in number, and were deemed by HIARC to be not of toxicological significance. Thus, HIARC did not select an acute endpoint for hydroxyatrazine, and concludes that no toxicologically significant endpoint to represent a single exposure can be found in the toxicology database for hydroxyatrazine. For chronic toxicity, the NOAEL selected for risk assessment by HIARC was 1.0 mg/kg/day, based on kidney alterations caused by the formation of hydroxyatrazine crystals in the blood at the next highest dose, the LOAEL of 7.5 mg/kg/day. This endpoint, which is based on entirely different effects than the parent compound, is comparable to NOAEL of 1.8 mg/kg/day used for the atrazine chronic risk assessment.

3.2 Food Quality Protection Act (FQPA) Considerations

Atrazine and the Chlorinated Metabolites
The FQPA Safety Factor Committee following review of the hazard and exposure (food, water and residential) data recommended that the FQPA safety factor be retained at 10x when assessing parent atrazine and its chloro-metabolites (represented by DACT) based on the following factors:

- There is qualitative evidence of increased susceptibility, given the prostate inflammation and delay in puberty in rat studies (in males and females with atrazine and in males with DACT), which are consistent with the atrazine's mode of action;

- There is cause for concern for infants and children given the evidence from special studies describing the central nervous system (CNS) mode of action (specifically, neuroendocrine alterations at the hypothalamus);

- Quantitative increased susceptibility was demonstrated in a prenatal developmental toxicity study with DACT in rats (developmental effects were seen in the absence of maternal toxicity);

- There is uncertainty in the toxicology data base and HIARC recommended that studies examining the CNS alterations be performed. Additionally, the HIARC required that a two-generation study be conducted with DACT employing the OPPTS Series 870 guidelines; and

- There is some uncertainty in the water monitoring data for the estimation of degradates in surface water and, to a greater extent, in ground water.

The FQPA safety factor for atrazine and its chlorinated metabolites is applicable to all population subgroups for dietary and non-dietary exposure assessments of all durations since there are concerns and uncertainties in the toxicology and exposure data bases which could impact all population subgroups during all durations of exposure.

Hydroxyatrazine

The FQPA Safety Factor Committee following review of the hazard and exposure (food, water and residential) data recommended that the FQPA safety factor be removed (1x) when assessing the hydroxy-metabolites since:

- There was no evidence of increased susceptibility in the prenatal developmental toxicity study in rats with hydroxyatrazine;

- There is no evidence of neurotoxicity from the submitted toxicity studies;

- The neuroendocrine effects described for atrazine are postulated to be part of a cancer mode of action for atrazine. Because hydroxyatrazine is non-carcinogenic, the current belief is that the neuroendocrine effects described for atrazine are not occurring following hydroxyatrazine exposure;

- The dietary and non-dietary exposure assessments do not underestimate the potential exposures for infants and children; and

- The drinking water exposure concerns expressed for atrazine and the chlorinated metabolites do not apply to hydroxyatrazine, given its dissimilar toxicological profile and environmental fate properties that indicate that hydroxyatrazine is less mobile in soil/water systems.

3.3 Dose Response Assessment

The toxicity endpoints selected for risk assessments conducted for atrazine and the chlorinated metabolites are presented in Table 2. The toxicity endpoints selected for risk assessment for hydroxyatrazine are presented in Table 3. Risk assessments included in this document are: an acute dietary assessment (combining a distributional analysis of one-day exposures to atrazine and the

chlorinated metabolites in food with a deterministic analysis of high-end, one-day exposures to atrazine and the chlorinated metabolites in drinking water), a chronic dietary assessment (combining a deterministic analysis of average exposures to atrazine and the chlorinated metabolites in food with seasonal and average annual exposures to atrazine and the chlorinated metabolites in drinking water), a short-term assessment based on non-occupational (residential) exposures of less than 30 days, and risk assessments for short- and intermediate-term occupational exposure scenarios.

3.3.1. Atrazine and the Chlorinated Metabolites

a. Acute Reference Dose (aRfD)

The acute RfD is used to assess acute dietary risk based on one-day oral exposures to atrazine and the chlorinated metabolites in the diet. An acute RfD of 0.10 mg/kg/day was derived from the NOAEL of 10 mg/kg/day and an uncertainty factor of 100 to account for inter-species variation and intra-species extrapolation. The NOAEL was based on delayed ossification seen at 70 mg/kg/day (LOAEL). This acute RfD is supported by other developmental studies (delayed puberty, and prolactin suppression induced prostatitis) consistent with atrazine's neuroendocrine mode of action.

The dose and endpoint was selected based on a weight of evidence approach using four studies; 3 of the 4 studies evaluated the developmental toxicity potential in two strains of rats (Charles River (CR) and Sprague Dawley) and the other was conducted with New Zealand White rabbits. The fourth, (a non-guideline study), examined the effects of maternal atrazine exposure during lactation on prostate effects in male suckling offspring. The recent pubertal assays in rats also support the acute RfD.

The high-level dose in the study using SD rats was 100 mg/kg/day, and mid-level dose in the study using CR rats was 70 mg/kg/day. The next lowest dose tested in study using the SD rat was 25 mg/kg/day; it was 10 mg/kg/day in the study using the CR rats. No observable adverse effects were seen at the 25 and 10 mg/kg/day dosing levels. Because skeletal anomalies such as delayed ossification of certain cranial bones (structures) were seen in each of the studies, respectively, at or above 70 mg/kg/day, and no observable adverse effects were seen at doses at or below 25 and 10 mg/kg/day, a developmental LOAEL of 70 mg/kg/day and NOAEL of 10 mg/kg/day were selected from these studies based on delayed ossification of cranial bones. The maternal LOAEL and NOAEL were 70 mg/kg/day and 10 mg/kg/day, respectively, based on reduced body weight gain.

The developmental study using rabbits gave very similar results and supports the selection of the LOAEL/NOAEL based on the rat studies. A somewhat wider dosing regime was used in the rabbit study with the high dose tested at 75 mg/kg/day and the next lowest dose tested at 5 mg/kg/day confirmed the results in the rat studies. No observable adverse maternal or fetal effects attributable to atrazine exposure were seen in the mid (5 mg/kg/day) and low (1 mg/kg/day) dose groups tested; however, the high dose group showed evidence of reduced body weight gain in the dams, and delayed ossification in the offspring.

An additional developmental effect was identified from a study taken from the open literature designed to test for hyperprolactinemia in rats. This is a condition that if it occurs prior to puberty in male rats may lead to lateral prostate inflammation in young adult male rats. A possible cause of this condition is a deficiency in milk-derived prolactin from a nursing mother. This effect is most critical the first week after birth in the rat. If the developing male offspring does not receive sufficient prolactin from the mother during the first week of its life, it may result in prostatitis in the adult. Maternal exposure to atrazine in the first week after birth was shown to inhibit the release of suckling-induced prolactin into the mother's milk, which reduces the amount of prolactin received by the suckling male rat, and ultimately leads to an increase in the incidence of lateral prostate inflammation. This effect was seen in all nursing dams at a 50 mg/kg/day dose, and for some but not others at the 25 and 12.5 mg/kg/day doses. This effect was not observed in any of the dams at the 6.25 mg/kg/day dose.

Although the lowest NOAEL seen in the above studies was 5 mg/kg/day, which is the developmental NOAEL from the rabbit developmental toxicity study, and the NOAEL from this study would be acceptable for use as an acute RfD, HIARC noted that there was a large dose spread between the high and mid-doses tested in this study. The mid-dose tested (and the NOAEL) in this study was 5 mg/kg/day while the next highest dose tested (the highest dose tested and the LOAEL) was 75 mg/kg/day. This dose is a full 15 times higher than the mid-dose tested. The large spread between 5 and 75 mg/kg/day raises the possibility that had intermediate doses between 5 and 75 been used then the NOAEL would have been higher.

In further support of the NOAEL selected as the basis of the acute RfD, examination of the rat developmental toxicity studies indicates that intermediate doses in the rabbit study between 5 and 75 may not have shown any adverse effects. The NOAEL in both the rat studies are greater than 5 mg/kg/day, 10 mg/kg/day and 25 mg/kg/day, respectively. The effects seen in the rabbit and two rat developmental toxicity studies are similar with all three studies showing delayed or no ossification in certain cranial bones at their respective LOAELs of 75 mg/kg/day in the rabbit, 70 mg/kg/day in the rat, and 100 mg/kg/day in the rat. Other effects on which the developmental NOAEL were based in the rabbit study - reduced litter size and increased resorptions - were not seen either of the rat studies and are not considered to be frank malformations, or even variations. In this respect it should be noted that maternal effects were more severe at the LOAEL in the rabbit study than at the LOAELs in either of the two rat studies. The maternal LOAELs in the two rat studies were based on decreased food consumption and body weight, while the maternal LOAEL in the rabbit study was based on clinical signs such as none, little or soft stool, blood on the vulva, in addition to decreased food consumption and body weight. The HIARC also noted that this acute RfD derived from the NOAEL of 10 mg/kg/day would be protective of the prostatitis effects seen in the open literature study at a NOAEL of 12.5

The weight-of-the-evidence for developmental effects taken from the four studies described above form the basis of the selection of the endpoint for acute risk assessment. The developmental effects seen in the two rat and one rabbit developmental studies are assumed to have the potential to occur after a single dosing. The effects seen in the open literature prostatitis paper occur after only 4 days of dosing.

Since the endpoints of concern, delayed ossification and prostatitis, were seen *in utero and post-natally as a result of lactation*, respectively, these endpoints are appropriate for the population subgroup females 13 to 50 years of age, only. An appropriate endpoint for the general population including infants and children was not available from the available oral toxicity studies including the developmental toxicity studies in rats and rabbits. Although there is exposure, the lack of hazard indicates that there is no potential risk from a single oral dietary exposure for the general population including infants and children

b. Chronic Reference Dose (cRfD):

The chronic RfD is used to assess chronic dietary risk based on oral exposures of several months to lifetime to residues of atrazine and the chlorinated metabolites in the diet (food and drinking water). A chronic RfD of 0.018 mg/kg/day was derived from the NOAEL of 1.8 mg/kg/day and an uncertainty factor of 100 to account for inter-species variation and intra-species extrapolation. The NOAEL was based on attenuation of LH surge at 3.65 mg/kg/day (LOAEL).

The toxicity database available for the selection of this endpoint for chronic risk assessment was complete and of high quality. Estrous cycle alterations and luteinizing hormone (LH) surge attenuation levels of the in female Sprague-Dawley rats form the basis of the chronic toxicity endpoint selected for chronic dietary exposures. In a special non-guideline study designed to evaluate the effect of long-term atrazine exposure on the proestrous afternoon luteinizing hormone (LH) surge atrazine was administered to 360 female Sprague Dawley rats in the diet at the following dose levels: 0, 1.8, 3.65, 29.44 mg/kg/day for approximately six months. This dose spacing was considered moderately steep.

Body weight, body weight gain and food consumption were significantly (p#0.05) decreased in animals receiving the highest dose compared to controls. Body weights decreased by 8.5% at the end of the study and food consumption decreased 3.75% for the entire study. The percentage of days in estrus were significantly increased (p#0.01) during the 21-22 and 25-26 week time periods at the highest dose tested. The percentage of days in estrus were also increased during the 21-22 and 25-26 week time periods at the mid dose tested, but the increase was only significant (p#0.05) for the 21-22 week time period. The proestrous afternoon LH surge was severely attenuated at the high dose where LH levels at most sampling time points were actually decreased compared to baseline. LH levels were attenuated at the mid dose, but less so, where the maximum increase in LH levels above baseline was 157% compared to a maximum increase over baseline in controls of 273%. Pituitary gland weights were increased at the high dose (absolute weight increased 22% and weight relative to body weight was increased 28%). Pituitary gland weights at the other two doses were not affected. There was a slight increase at the high dose of animals displaying enlarged pituitaries (0% in controls compared to 3.4% at 29.44 mg/kg/day) and thickened mammary glands (0% in controls compared to 6.7% at 29.44 mg/kg/day). There were no other gross necropsy findings in the animals receiving the high dose that could be attributed to compound exposure, and there were no compound-related gross pathology findings at either the mid dose or low dose. Selected tissues were saved for histopathology but those

results have yet to be reported. There were no compound related effects in mortality or clinical signs. The proestrous afternoon prolactin surge was not affected by compound exposure at any dose. The lowest dose tested of 1.8 mg/kg/day had no effects on the estrous cycle, LH or prolactin surges.

The attenuation of the LH surge is deemed to be a critical event in the mode of action of atrazine-associated carcinogenesis in the Sprague-Dawley strain of rat. This six-month study is considered adequate for use in selecting a chronic endpoint without an additional safety factor being added to account for study duration of less than 12 months. A LH surge study of longer duration may be of limited value given that the attenuation of LH surge occurs in normally aging Sprague-Dawley rats around 9 months of age. Though this endpoint (LH surge attenuation and estrous cycle disruption) is applicable only to females 13-50, HED's HIARC noted that this dose is the lowest NOAEL available in the toxicology database (i.e., the most sensitive endpoint), and therefore would be protective of other adverse effects, including those occurring in males, infants and children. Further, the attenuation of the LH surge is considered a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function in general. Therefore, a separate endpoint was not selected for other populations (i.e., males, infants and children).

This dose and endpoint replaces the previous dose and endpoint of 3.5 mg/kg/day based on decreased body weight gain and food consumption in a two-year rat bioassay selected by HIARC in 1998. The dose of 1.8 mg/kg/day for use in risk assessment would be protective of effects that occur at the higher dose of 3.5 mg/kg/day as well as protective of effects such as LH surge attenuation and estrous cycle alterations, and any effects that may be associated with alteration of these parameters.

This endpoint is particularly appropriate for assessing intermediate-term and chronic exposures to atrazine in drinking water, as these exposures occur both as seasonal pulses from weeks to months in duration, and chronically from months to years in duration, reflective of atrazine's use patterns and occurrence in drinking water.

c. Short-Term Oral Exposures

For assessing the short-term (1 to 30 days) risks from incidental oral exposures of toddlers, the HIARC selected the maternal NOAEL of 10 mg/kg/day based on decreased body weights seen during the first five days of dosing in the developmental toxicity study in rats. This dose and endpoint, indicative of general or systemic toxicity, is appropriate for toddlers, who are the relevant population subgroup of interest under this exposure scenario and risk assessment.

d. Intermediate-Term Oral Exposures

For assessing the intermediate-term (30 days to several months) risks from incidental oral exposures of toddlers, the HIARC selected the NOAEL of 1.8 mg/kg/day based on attenuation of the LH surge used as a biomarker for alterations of hypothalamic-pituitary function from a sub chronic toxicity study in rats.

This dose and endpoint, indicative of indicative of atrazine's ability to alter hypothalamic-pituitary function, in general, is appropriate for toddlers, the relevant population subgroup of interest under this exposure scenario and risk assessment.

e. Dermal Absorption.

Dermal absorption studies are available both in rats and human and therefore a dermal penetration factor has been calculated. The available data indicates that skin permeability of atrazine is lower in humans than in rats. It is not uncommon for humans to have lower skin permeability to many compounds compared to rats. The stratum corneum known to absorb many compounds and serve as a reservoir of absorbed compound from which a compound steadily diffuses across the epithelium into the dermis is much thicker in rats than in the human resulting in this reservoir being a much greater factor to the rat than to the human. As a result rat dermal absorption frequently is much greater than human dermal absorption.

In the dermal absorption study with rats, dermal absorption was determined to be 22% based on absorption of the 0.1 mg/kg/day single dose left on the skin for 10 hours prior to wash-off, and then allowed to continue to adsorb for 82 hours prior to sacrifice. This value is selected because it represents the highest dermal absorption value seen following a 10 hour exposure (approximating a typical human workday) in the rat study. The majority of the dose applied to the skin was recovered in washes (65-95%) depending on the length of time the dose was left on the skin prior to wash-off.

In the dermal absorption study with humans, dermal absorption was estimated to be 6% based on the highest percent absorbed in this study.

A dermal penetration factor of 3.6 was calculated by dividing the 22% dermal absorption in the rats by the 6% dermal absorption in the humans (22%÷6% = 3.6) to account for this species differences in rates of dermal absorption between rats and humans. When a dermal dose is selected from a dermal toxicity study, this dose is then multiplied by the dermal penetration factor to account for the absorbed dose but not when an oral dose is selected in which case a dermal absorption factor should be used for route-to-route extrapolations.

f. Short-Term (1 to 30 Days) Dermal Exposure

For short-term dermal exposure risk assessments, the HIARC selected the systemic short-term effect of decreased body weight gain based on a NOAEL of 100 mg/kg/day established in the 21-day dermal toxicity study in rabbits. As stated earlier, since the dose is from a dermal toxicity study, the 3.6 dermal penetration factor is used to yield a dermal absorbed dose of 360 mg/kg/day (100 x 3.6 =360) for risk assessments. The 21-day dermal toxicity study in rabbits was considered appropriate since the route (dermal) and duration (15 applications) of treatment under experimental conditions simulate the actual worker exposure scenario (dermal exposure up to one week).

In the 21-day dermal toxicity study, rabbits received 15 repeated dermal applications of atrazine which resulted in minimal to moderate acanthosis, hyperkeratosis, and focal subacute inflammation of treated skin in high-dose females. Dermal irritation included slight erythema and scaling in one high dose female at days 17 to 25. Slight erythema was observed in one high dose male at day 18. For systemic toxicity, the NOAEL was 100 mg/kg/day based on based on clinical signs of toxicity, and statistically significant reductions in food consumption, mean body weight, body weight gain and increases in absolute and relative spleen weights in both sexes at 1000 mg/kg/day (LOAEL).

g. Intermediate-term (30 days to Several Months) and Long-term (Several Months to Life-Time) Dermal Exposure

For intermediate- and long-term dermal exposures into risk assessments, the HIARC determined that the 21-day dermal toxicity study is not appropriate since the principal toxicological effect of concern (i.e., attenuation of LH surge) seen after 3 to 6 months of exposure is the endpoint of concern for these exposure scenarios, and this effect was neither measured in this species (rabbits) or this study. Therefore, the oral NOAEL of 1.8 mg/kg/day based on the attenuation of LH surge was selected for these risk assessments. Since an oral NOAEL was selected, the 6% dermal absorption factor has been used in route-to-route extrapolation.

h. Inhalation exposure

With the exception of an acute inhalation study, no inhalation studies are available for evaluation. Therefore the HIARC selected oral NOAELs for short, intermediate and long-term inhalation exposure risk assessments. For short-term inhalation exposure, the dose and endpoint of concern is the NOAEL of 10 mg/kg/day based on decreased body weight gain, and for intermediate-term exposure and long-term (chronic) exposure, the dose and endpoint of concern is the NOAEL of 1.8 mg/kg/day based on attenuation of LH surge as a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function, in general. A 100% inhalation absorption will be used for route-to-route extrapolations.

i. Aggregate Exposure

For risk assessments aggregating short-term exposures, the oral, dermal, and inhalation exposures can be combined since the endpoint (statistically significant decreases in body weight gains) is common via these routes. For intermediate-term and long-term (chronic) risk assessments, the oral, dermal, and inhalation exposures can be combined because they are based on oral equivalents from the same toxic effect (attenuation of LH surge as a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function in general).

j. Cancer Classification

In accordance with the 1999 Draft Guidelines for Carcinogen Risk Assessment, the CARC classified

atrazine as “not likely to be carcinogenic to humans”. The attenuation of the LH surge and estrous cycle disruptions appears to be a species, strain and sex specific effect occurring only in female Sprague-Dawley rats. The Agency's FIFRA Scientific Advisory Panel (SAP) convened in June 2000 determined that it is unlikely that atrazine's cancer mode of action in the SD rat is operative in humans. HED's Cancer Assessment Review Committee (CARC) also concluded that the mode of action is not relevant to humans. Although hypothalamic disruption of pituitary function (i.e., attenuation of the LH surge) and resulting estrous cycle disruption may be occurring in humans following atrazine exposure, the hormonal environmental resulting from these events would be expected to be much different from the environment seen in the rat. The prolonged/increased exposure to estrogen and prolactin seen in the rat would not be expected to occur in humans. Consequently, a cancer risk assessment was not conducted for atrazine.

Table 2. Toxicology Endpoint Selection Table for Atrazine			
EXPOSURE SCENARIO	**DOSE (mg/kg/day)**	**ENDPOINT**	**STUDY**
Acute Dietary (females 13 to 50 years of age)	NOAEL= 10 UF = 100 FQPA SF = 10	Delayed ossification of certain cranial bones in fetuses (LOAEL = 70 mg/kg/day). Decreased body weight gain in adult (LOAEL = 70 mg/kg/day).	Developmental toxicity study in rat & rabbit (weight of evidence from four studies)
	Acute RfD = 0.1 mg/kg/day **Acute PAD** = 0.01 mg/kg/day		
Chronic Dietary (all populations)	NOAEL = 1.8 UF = 100 FQPA SF = 10	Attenuation of pre-ovulatory lutenizing hormone (LH) surge, as a biomarker indicative of hypothalamic function disruption (LOAEL = 3.65 mg/kg/day)	Six-month LH surge study -Rat
		Chronic RfD = 0.018 mg/kg/day **Chronic PAD** = 0.0018 mg/kg/day	
Oral, Short-Term (toddlers)	NOAEL= 10 UF = 100 FQPA SF = 10	Decreased body weight gain during the first five days of dosing in the dams (LOAEL = 70 mg/kg/day)	Developmental toxicity study in rat & rabbit (weight of evidence from four studies)
Oral, Intermediate-Term (toddlers)	NOAEL = 1.8 UF = 100 FQPA SF = 10	Attenuation of pre-ovulatory lutenizing hormone (LH) surge, as a biomarker indicative of hypothalamic function disruption (LOAEL = 3.65 mg/kg/day)	Six-month LH surge-Rat
Dermal, Short-Term[a] (all populations)	NOAEL= 360 UF = 100 FQPA SF = 10	Reductions in mean body weight, body weight gain, increases in absolute and relative spleen weights in both sexes. Use of the 3.6 dermal penetration factor yields a dose of 360 mg/kg/day. (LOAEL = 1000 mg/kg/day)	21-day Dermal toxicity-Rabbit
Dermal, Intermediate- and Long-Term[b] (all populations)	NOAEL= 1.8 UF = 100 FQPA SF = 10	Attenuation of pre-ovulatory lutenizing hormone (LH) surge, as a biomarker indicative of hypothalamic function disruption (LOAEL = 3.65 mg/kg/day)	Six-month LH surge-Rat
Inhalation, Short-Term [c] (all populations)	NOAEL= 10 UF = 100 FQPA SF = 10	Decreased body weight gain during the first five days of dosing in the dams (LOAEL = 70 mg/kg/day)	Developmental toxicity -Rat
Inhalation, Intermediate and Long-Term [c] (all populations)	NOAEL= 1.8 UF = 100 FQPA SF = 10	Attenuation of pre-ovulatory lutenizing hormone (LH) surge, as a biomarker indicative of hypothalamic function disruption (LOAEL = 3.65 mg/kg/day)	Six-month LH surge-Rat

a = The NOAEL of 100 mg/kg/day is multiplied by a 3.6 dermal penetration factor.
b = Use 6% dermal absorption factor for route-to-route extrapolation.
c = Use 100% dermal absorption factor for route-to-route extrapolation.
MOE= Residential = A MOE of 1000 is required and includes the 10x FQPA Safety Factor
Occupational = A MOE of 100 is adequate
PAD = Population Adjusted Dose

3.3.2. Hydroxyatrazine

Hydroxyatrazine is a metabolite of atrazine. Plants are capable of metabolizing atrazine to hydroxyatrazine. In plants it is the major metabolite. Bacteria are also able to metabolize atrazine to hydroxyatrazine. Animals do not metabolize atrazine to hydroxyatrazine. However, animals may receive hydroxyatrazine in their diets through forages and fodders.

Toxicity studies submitted under Subdivision F Guideline requirements (i.e., subchronic, chronic/carinogenicity, and developmental) indicates that the kidney is the primary target organ for hydroxyatrazine associated toxicity. Hydroxyatrazine appears to crystallize in the serum leading to the formation in the blood stream of hydroxyatrazine crystals. These crystals cause direct physical damage to the kidney. This crystallization phenomenon has not been observed with atrazine or any of the chlorinated metabolites of atrazine. Hydroxyatrazine is not a chlorinated metabolite of atrazine, and is not expected to be associated with any of the effects attributed to atrazine or its chlorinated metabolites.

There is no evidence for increased susceptibility of rat fetuses following *in utero* exposure to exposure to hydroxyatrazine in the prenatal developmental toxicity study in rats. However, neither a prenatal developmental study in the rabbits nor a two-generation reproductions study conducted with hydroxyatrazine in rats is available. In the prenatal developmental toxicity study in rats there was a statistically significant decrease in fetal weights and an increase in incompletely ossified interparietals and hyoid bones was seen in the presence of maternal toxicity. HIARC determined that these findings lacked toxicologic significance. While special studies and an open literature study indicate a neuroendocrine toxicity in the CNS of rats following atrazine exposure, overt signs of neurotoxicity were not seen in the toxicology studies for hydroxyatrazine. The neuroendocrine alterations mentioned above would not be expected to be seen following hydroxyatrazine exposure.

Hydroxyatrazine was non mutagenic with or without metabolic activation in revertant colonies of four *Salmonella* strains exposed to hydroxyatrazine. The metabolite did not cause an increase in micronuclei in mice in the in vivo mouse micronucleus assay. No evidence of unscheduled DNA synthesis was found in primary hepatocyte cultures treated *in vitro* with hydroxyatrazine. Negative results were reported in human fibroblast cells treated with hydroxyatrazine

Food Quality Protection Act (FQPA) Considerations

The FQPA Safety Factor Committee following review of the hazard and exposure (food, water and residential) data recommended that the FQPA safety factor be removed (1x) when assessing the hydroxy-metabolites since:

- There was no evidence of increased susceptibility in the prenatal developmental toxicity study in rats with hydroxyatrazine;

- There is no evidence of neurotoxicity from the submitted toxicity studies;

- The neuroendocrine effects described for atrazine are postulated to be part of a cancer mode of action for atrazine. Because hydroxyatrazine is non-carcinogenic, the current belief is that the neuroendocrine effects described for atrazine are not occurring following hydroxyatrazine exposure;

- The dietary and non-dietary exposure assessments do not underestimate the potential exposures for infants and children; and

- The drinking water exposure concerns expressed for atrazine and the chlorinated metabolites do not apply to hydroxyatrazine, given its dissimilar toxicological profile and environmental fate properties that indicate that hydroxyatrazine is less mobile in soil/water systems.

a. Acute Reference Dose (aRfD):

A toxicological endpoint attributable to a single exposure (dose) was not identified in the available toxicology database to establish an acute RfD. The only effects seen in any of the studies which may be attributable to a single dose were the development alterations in the developmental rat study which were seen only at the high dose, were few in number, and were not deemed by HIARC to be of toxicological significance. No other study in the database was found to have effects which could be attributed to a single exposure. Thus, HIARC concludes that no toxicologically significant endpoint to represent a single exposure can be found in the toxicology database for hydroxyatrazine.

b. Chronic Reference Dose (cRfD)

The chronic RfD is used to assess chronic dietary risk based on long-term oral exposures to residues of atrazine's hydroxy metabolites in the diet. A chronic RfD of 0.01 mg/kg/day was derived from the NOAEL of 1 mg/kg/day and an uncertainty factor of 100 to account for inter-species variation and intra-species extrapolation. The NOAEL was based on histopathological lesions of the kidney at 7.75 mg/kg/day (LOAEL).

In a combined chronic/carcinogenicity study conducted with Sprague-Dawley (BR strain) rats, both male and female rats exhibited gross and histopathological effects in the kidneys. No treatment-related increases in incidences of tumors of any type was observed in the treated male or female animals in this study. In particular, there was no increase above control levels in the incidence of mammary gland tumors in either males or females. In addition, onset times for mammary gland tumors in female rats were not decreased in this study.

c. Dermal Absorption.

A dermal absorption study is not available with hydroxyatrazine. Therefore, the HIARC recommended that the 6% dermal absorption factor from atrazine should be used for hydroxyatrazine.

d. Short-Term (1 to 30 Days) Dermal and Inhalation Exposures

For short-term dermal exposure risk assessments, the HIARC selected the maternal NOAEL of 25 mg/kg/day based on decreased food consumption and renal effects in dams in the developmental toxicity study in dams. Since an oral NOAEL was selected, the 6% dermal absorption and 100% inhalation absorption factor was been used in route-to-route extrapolation.

e. Intermediate-term (30 Days to Several Months) Dermal and Inhalation Exposures

For intermediate- and long-term dermal exposures into risk assessments, the HIARC selected the oral NOAEL of 6.3 mg/kg/day based on the renal lesions in the subchronic toxicity study in rats for these risk assessments. Since an oral NOAEL was selected, the 6% dermal absorption and 100% inhalation absorption factor was been used in route-to-route extrapolation.

f. Long-term (Several Months to Life-Time) Dermal and Inhalation Exposures

For long-term dermal exposures into risk assessments, the HIARC selected the oral NOAEL of 1 mg/kg/day based on the renal lesions in the combined chronic toxicity/carcinogenicity toxicity study in rats for these risk assessments. Since an oral NOAEL was selected, the 6% dermal absorption and 100% inhalation absorption factor was been used in route-to-route extrapolation.

g. Aggregate Exposure

Although a risk assessment for exposures to atrazine's hydroxylated metabolites in food was conducted, risk assessments aggregating exposures to atrazine's hydroxylated metabolites in food, drinking water, and in residential settings have not been conducted. There is only limited data on hydroxyatrazine in water and exposure to the hydroxy metabolites of atrazine relative to the chlorinated metabolites is not expected to be significant in drinking water. Exposure to hydroxyatrazine from applications of atrazine to turf in residential settings is not expected. Hydroxyatrazine is formed within plant tissues once the atrazine has been absorbed into plant tissues and metabolized, and is not excpected to form on plant surfaces.

h. Cancer Classification:

Hydroxyatrazine has not been classified as to its carcinogenic potential by the HED Cancer Peer Review committee. The HED Metabolism Committee concluded in a September 29, 1995 meeting that: "For

atrazine, the residues of concern for cancer dietary risk are parent and chloro- metabolites". Hydroxyatrazine is not a chloro-metabolite of atrazine, and is not considered by the HED metabolism committee to possess carcinogenic potential.

Table 3. Toxicology Endpoint Selection for Hydroxyatrazine

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	None selected	An appropriate endpoint attributable to a single dose was not identified	None selected
	Acute RfD = Not Established		
Chronic Dietary	NOAEL = 1.0 UF = 100 FQPA SF = 1	Histopathological lesions of the kidneys (LOAEL = 7.75 mg/kg/day)	Combined chronic toxicity/carcinogenicity -Rat
		Chronic RfD = 0.01 **Chronic PAD** = 0.01 mg/kg/day	
Dermal, Short-Term [a]	NOAEL= 25 UF = 100 FQPA SF = 1	Decreased food consumption and renal effects in the dams (LOAEL = 125 mg/kg/day)	Developmental toxicity -Rat
Dermal, Intermediate-Term[a]	NOAEL= 6.3 UF = 100 FQPA SF = 1	Histopathological lesions of the kidneys (LOAEL = 22.75 mg/kg/day)	90-day study-Rat
Dermal, Long-Term [a]	NOAEL= 1.0 UF = 100 FQPA SF = 1	Histopathological lesions of the kidneys (LOAEL = 7.75 mg/kg/day)	Combined chronic toxicity/carcinogenicity -Rat
Inhalation, Short-Term[a]	NOAEL= 25 UF = 100 FQPA SF = 1	Decreased food consumption and renal effects in the dams (LOAEL = 125 mg/kg/day)	Developmental toxicity -Rat
Inhalation, Intermediate-Term[b]	NOAEL= 6.3 UF = 100 FQPA SF = 1	Histopathological lesions of the kidneys (LOAEL = 22.75 mg/kg/day)	90-day study -Rat
Inhalation, Long-Term[b]	NOAEL= 1.0 UF = 100 FQPA SF = 1	Histopathological lesions of the kidneys (LOAEL = 7.75 mg/kg/day)	Combined chronic toxicity/carcinogenicity -Rat

a = Use 6% dermal absorption factor for route-to-route extrapolation.
b = Use 100% dermal absorption factor for route-to-route extrapolation.
MOE= 100 for Occupational; no potential exposure under residential settings.

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Registered Uses

Atrazine (2-chloro-4-ethylamino-6-isopropylamino-*s*-triazine) is a triazine herbicide registered in the

United States by Novartis Crop Protection, Inc. under the trade names Aatrex® and Bicep® for the control of annual broadleaf weeds in corn (field and sweet), guavas, macadamia nuts, sorghum, sugarcane, range grasses, and wheat (where application is to wheat stubble on fallow land following wheat harvests; wheat is not the target crop). Although not currently supported by the primary producer, tolerances for orchard grass and hay exist. HED recommends that these tolerances for orchard grass and hay be revoked. Atrazine is also registered for use on commercial (golf courses) and residential lawns for the control of broadleaf weeds in southern turf grasses. Because of the specific nature of the lawn uses, much of atrazine's use on lawns is confined to Florida and the Southeast.

Atrazine formulations registered to Novartis for use on food/feed crops include flowable concentrate (FlC) and water dispersable granular (dry flowable, DF) formulations. These products may be applied as a broadcast or banded preemergence, preplant, or early postemergence application using either ground or aerial equipment. Most of the currently registered formulations are formulated as flowable concentrates ranging from 1.67 lbs/gallon to 4 lbs/gallon as shown in Table 4.

Table 4. End-Use Products with Food/Feed Uses Registered to Novartis Crop Protection, Inc.

EPA Reg No.	Label Acceptance Date	Formulation Class	Product Name
100-497 [a]	8/98	4 lb/gal FlC	Atrex® 4L Herbicide
100-585 [b]	8/98	90% DF	Atrex Nine-0® Herbicide
100-817[c]	4/99	3.1 lb/gal FlC	Bicep II MAGNUM® Herbicide
100-827[d]	5/99	2.67 lb/gal FlC	Bicep Lite II MAGNUM® Herbicide
100-886[e]	2/98	3.1 lb/gal FlC	Bicep MAGNUM® Herbicide
100-928[f]	11/98	2.0 lb/gal FlC	Bicep MAGNUM TR® Herbicide

[a] Includes SLN Nos. FL 80002400; IA970001; KS980003; MN0000040; OK830003; OK930004; OK830029; OK910003; OK920007; and TX920005.

[b] Includes SLN Nos. ID830009; OK830003; OK910001; OK920008; OK910001; OK930005; OR790077; OR8000100; TX920006; VT80008; WA790078; WA800083.

[c] A MAI that also includes *S*-metolachlor (2.4 lb/gal FlC) in addition to 3.1lb/gal of atrazine.

[d] A MAI that also includes *S*-metolachlor (3.33 lb/gal FlC) in addition to 2.67 lb/gal of atrazine.

[e] A MAI that also includes CGA-77102 (2.4 lb/gal FlC) in addition to 3.1 lb/gal of atrazine.

[f] A MAI that also includes *S*-metolachlor (2.5 lb/gal FlC) and flumetsulam (0.09 lb/gal FlC) in addition to 2.0 lb/gal of atrazine.

Although there are some post-emergence uses, atrazine, in general, is primarily used in early spring pre-plant and pre-emergence soil applications. Corn is treated with atrazine preplant, pre-emergence and post-emergence before the corn plant is 12 inches tall. About 70% of the corn crop is treated pre-plant or pre-emergence and about 30% is treated post-emergence. Average seasonal treatment rates are 1 to 1.5 lbs ai/acre with a maximum treatment rate of 2.5 lbs ai/acre. Sorghum use is similar, with an average seasonal use rate of 1.2 lbs ai/acre, and a maximum use rate of 2.5 lbs ai/acre. About 75% of the use on sorghum is pre-emergence and 25% is post-emergence. Atrazine is used both pre- and post-emergent on sugarcane at an average of 4 lbs ai/acre/sugar crop, and a maximum of 10 lbs ai/acre/sugar crop. On wheat, atrazine can be applied to fallow fields up to 1 lb ai/acre/year in a wheat-fallow-wheat rotation. Atrazine is used on macadamia nuts at a maximum of 2 to 4 lbs ai/year as needed, and on guava at a maximum 8 lbs ai/acre/year.

Currently, there are four products with labeled uses on pasture land and rangeland on terrestrial feed items (forages and fodder) or for road side (right-of-way) uses. Valent Atrazine 90DF (59639-106), Riverside Atrazine 90 DF (9779-253) and Oxon Italia 5 L (35915-5) are labeled for application to roadsides at 2 pints per acre, and allow application to Conservation Reserve Program (CRP) land in NE, OR, OK, and TX at 2.2 lbs product/acre. Drexel Atrazine 4L (19713-11) is labeled for roadside uses, only. Both of these use patterns include prohibitions against grazing or cutting for hay. The orchard grass and hay use is unsupported by the registrant. HED does not support label restrictions against grazing or feeding.

4.2 Dietary Exposure

HED's dietary exposure assessment for atrazine includes anticipated exposures through food and drinking water.

4.2.1 Food Exposure

Adequate residue data are available to assess dietary exposure to atrazine. Anticipated residues (ARs) of atrazine and its chlorinated metabolites were estimated for comparison to the appropriate acute and chronic endpoints identified for atrazine. Anticipated residues of atrazine's four hydroxy metabolites were estimated for comparison to the appropriate chronic endpoint identified for hydroxyatrazine.

Monitoring data are available for atrazine, the parent compound only, for many foods. The USDA's Pesticide Data Program (PDP), Food and Drug Administration (FDA), and Food Safety and Inspection Service (FSIS) have all monitored for atrazine. In general, these monitoring data suggest that exposure to the parent atrazine through the diet is small. Because the parent atrazine is not found in any appreciable quantities in the fruiting parts of plants in the metabolism studies, it is difficult to estimate the total chloro- or hydroxy-metabolites in fruits, nuts or grains based upon testing for parent atrazine, alone. Therefore, for dietary exposure assessments, residues of atrazine, its chloro-and hydroxy metabolites were estimated mostly from field trial and metabolism study data where possible as these studies included analyses for the chloro- and hydroxy-metabolites, as well as the parent compound, in the main crops on which atrazine is used. Except for sugar cane, all human foods treated with atrazine are fruits, nuts or grains. Sugar cane is highly processed before it is consumed by humans.

Plant and Animal Metabolism:

Plant and animal metabolism of atrazine is well understood. In general, atrazine is metabolized in plants through replacement of the chloro-atom with either a hydroxy group or by a glutathione conjugate. This leads to three families of metabolites: the chlorinated metabolites, the hydroxy-metabolites, and the glutathione metabolites. Within each family, three additional metabolites can arise by removal of either one or both of the N-alkyl moieties. Other metabolites can also arise within the glutathione family of metabolites by metabolic changes to the glutathione conjugate.

All of the major modes of metabolism described above have been identified in plants and can be summarized as replacement of the chloro-atom with a hydroxy-group (hydrolytic dehalogenation),

glutathione conjugation, and removal of either one or both of the N-alkyl groups (dealkylation). All routes leave the central triazine ring intact, and, since these modes exist in competition, all three families of metabolites (chloro-, hydroxy-, and glutathione conjugates) can exist in combination with each of the N-dealkylated forms. Metabolism by hydrolytic-dehalogenation dominates for residues absorbed through the roots while metabolism by glutathione conjugation dominates for foliarly applied residues.

Atrazine's metabolism in animals is similar to plants. However it is dominated by removal of either one or both of the N-alkyl groups (dealkylation), and subsequent glutathione conjugation. Hydroxy metabolites of atrazine are not produced in tissues of animals dosed with atrazine, per se. As in plants, all metabolic routes in the animal leave the central triazine ring intact. The structures of atrazine and its chloro- and hydroxy-metabolites are given in Figure 2.

Figure 2. Atrazine and Major Plant and Animal Metabolites

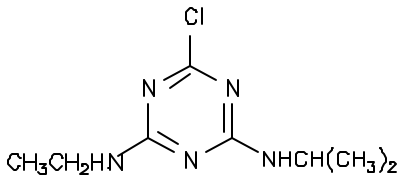
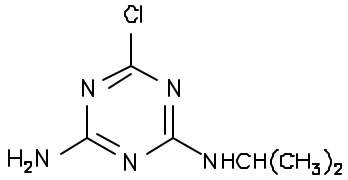
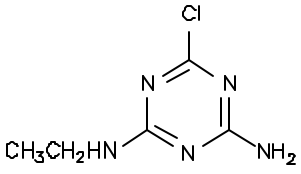
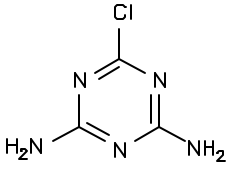
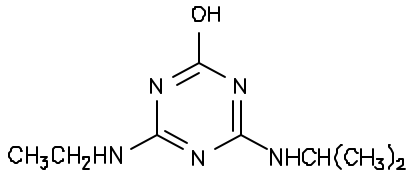
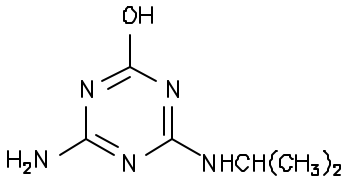
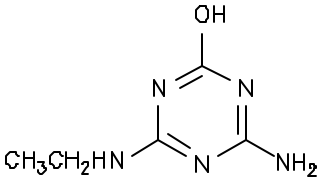
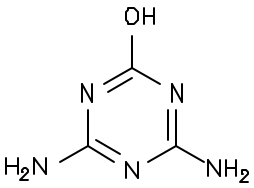
Common/Chemical Name (Code)	Chemical Structure
Atrazine 2-chloro-4-ethylamino-6-isopropylamino-*s*-triazine (G-30027)	
2-amino-4-chloro-6-isopropylamino-*s*-triazine (G-30033)	
2-amino-4-chloro-6-ethylamino-*s*-triazine (G-28279)	
2,4-diamino-6-chloro-*s*-triazine (G-28273)	

Figure 2. Atrazine and Major Plant and Animal Metabolites	
Common/Chemical Name (Code)	Chemical Structure
Hydroxyatrazine 2-hydroxy-4-ethylamino-6-isopropylamino-*s*-triazine (G-34048)	
2-amino-4-hydroxy-6-isopropylamino-*s*-triazine (GS-17794)	
2-amino-4-hydroxy-6-ethylamino-*s*-triazine (GS-17792)	
Ammeline 2,4-Diamino-6-hydroxy-*s*-triazine (GS-17791)	

Tolerance Reassessment and Residues to be Regulated:

Tolerances are established for residues of the herbicide atrazine, 2-chloro-4-ethylamino-6-isopropylamino-s-triazine, in or on agricultural plant and animal commodities (40 CFR 180.220(a)(1), and for combined residues of atrazine and its metabolites 2-amino-4-chloro-6-ethylamino-s-triazine (G-

28279), 2-amino-4-chloro-6-isopropylamino-s-triazine (G-30033), and 2-chloro-4,6-diamino-s-triazine (G-28273), in or on specified plant commodities (40 CFR 180.220(a)(2).

As a result of tolerance reassessment, HED's Metabolism Assessment Review Committee (MARC) has determined that the residues to be regulated by established tolerances in plant and animal commodities are atrazine and its chlorinated metabolites: desethyl atrazine (G-30033), desisopropyl atrazine (G-28279), and diaminochlorotriazine (G-27283). The HED MARC has also determined that separate tolerances must be established for residues of the hydroxyatrazine metabolites: G-34048, GS-17794, GS-17792, and GS-17791 in plants. Analytical methods are available to analyze for each of these compounds in plants and animals.

In general, the tolerance reassessment process resulted in a lowering of tolerances for most raw agricultural plant commodities and a slight raising of tolerances for animal commodities. The lowered tolerances on the plant commodities reflect seasonal use rate reductions in corn from 4 lbs ai/acre to 2.5 lbs ai/acre. The rise in tolerances for animal commodities reflects the HED MARC decision to include the chlorinated metabolites of atrazine in animal tolerances. Reassessed tolerances for atrazine can be found in HED's Product and Residue Chemistry Chapter for Atrazine (Attachment IV).

HED's Chemistry Science Assessment Committee determined that because there was no reasonable expectation of finite residues of atrazine, its chloro- and hydroxy-metabolites in tissues of hogs, or in poultry tissues and eggs, these commodities could be classified as 180.6(a)3, "no reasonable expectation of finite residues" (HED memoranda D269608 & D269514, C. Eiden, 10/15/00 & 10/05/00). HED recommends that the existing tolerances on *hogs, fat, hogs, meat, hogs, mbyp,* and *poultry fat, poultry meat, poultry mbyp,* and *eggs* under the 40 CFR 180.220(a)(1) be revoked. As the primary producer of atrazine is no longer supporting uses of atrazine on orchard grasses and orchard grass, hay, HED recommends that the established tolerances for residues in/on *orchard grass and orchard grass, hay* under the 40 CFR 180.220(a)(2) be revoked. HED recommends that existing tolerances be revoked for *sugarcane fodder and forage* under the 40 CFR 180.220(a)(1) because these are not significant livestock feed items. The commodities with tolerances recommended for revocation above have not been included in the dietary exposure assessments, as either animal feeds or human foods.

The HED MARC has determined that the atrazine residues of concern for acute dietary risk are the parent and chlorinated metabolites (memoranda: C. Eiden, 10/05/00, D269513 & C. Eiden, 11/15/00). The HED MARC has also determined that the residues of concern for chronic non-cancer dietary risk are: (i) combined free hydroxy metabolites, and (ii) parent and chlorinated metabolites. Separate chronic reference doses (RfDs) have been identified for each of these sets of residues for the purposes of chronic dietary exposure assessment. The group of metabolites that retain the chloro-atom, including parent and the three metabolites formed by loss of either or both N-alkyl groups from the parent are assumed to have the same toxicological effects as atrazine. Therefore, the dietary exposure and risk assessment has been conducted for the combined residues of atrazine and the chlorinated metabolites. Since, the HIARC has assigned a separate toxicological endpoint to hydroxyatrazine for risk assessment, a risk assessment for food exposures, only, has been conducted for the combined residues of atrazine's four hydroxy metabolites. The group of four hydroxy-metabolites is formed by replacement of the chloro-atom with a hydroxy-group plus loss of either or both N-alkyl groups. All four compounds are assumed

to have same toxicological effect and their combined residues have been compared to the endpoint specific to hydroxyatrazine in a separate risk assessment.

Although there are tolerances for range grasses, residues on range grasses were not included in the dietary assessment for meat and milk, as these uses are limited to 3.5 million acres under the Conservation Reserve Program (CRP) in OK, OR, NE, and TX. The CRP is administered by the USDA. Atrazine is applied to these lands to clear away existing grasses and allow the selected native grass to become established. As a result, applications of atrazine occur prior to planting the native grasses. Under this use, it is prohibited to use these lands for grazing and to cut the grasses for hay, except in national emergencies. Atrazine residues are expected to be insignificant by the time any native grass would be harvested for feed as in the case of a national emergency. Further, atrazine is used on at least 70% of the U.S. corn crop, which is estimated at 70 million acres annually. Since corn grain and forage are significant livestock feed items and are fed preferentially to beef cattle for fattening before slaughter, it is expected that atrazine residues in corn forage and grain impact the livestock diet to a greater degree than range grasses grown on CRP lands. Because of the limited acreage, timing of application, restrictions on the use of these range grasses for animal feeds, and the dominance of corn as a feed item, range grasses are not expected to impact either the livestock diet or the risk estimates significantly, and consequently were not included in the dietary exposure assessments.

Anticipated Residues used to Estimate Dietary Exposure:

Anticipated residues were derived in accordance with established Agency policies and guidance for chronic and acute dietary exposure assessments. Residues for chronic dietary exposure analyses are generally based on the mean of the best available residue data with appropriate adjustments for percent crop treated and residue concentration/reduction from processing. Acute anticipated residues were derived using guidance provided in HED SOP 99.6 (Classification of Food Forms with Respect to Level of Blending (8/20/99)). Anticipated residues in milk for use in acute and chronic dietary exposure assessments were determined in accordance with HED memorandum “Clarification of AR Calculation for Meat/Milk in Acute Assessments”, 10/14/99, D. Miller. Each food form included in the dietary exposure assessments is classified as being blended (B), partially blended (PB), or not blended (NB). The only food form included in the dietary risk assessments for atrazine as a non-blended form was guavas. However, since no residue data were available on guavas from either field trials or monitoring data, and tolerance level residues were entered into the dietary assessments, there was no need to decomposite monitoring data that may have been collected on composite samples of foods. The only monitoring data used in dietary assessments for atrazine were for wheat, which is a blended commodity, and therefore, there was no need to decomposite these monitoring data. The exact anticipated residue values used in the dietary exposure assessments and supporting calculations for each commodity are provided in HED's "Anticipated Residues and Acute and Chronic Dietary Exposure Assessments for Atrazine" (Attachment V).

Residue Data for Raw Agricultural Commodities:

The USDA’s Pesticide Data Program (PDP) monitored for atrazine, *per se*, in 1993 through 1997 in a wide variety of foods including peaches, pears, apples, bananas, grapes, oranges, apple juice, spinach,

wheat, green beans, potatoes, sweet corn, tomatoes, lettuce, and milk. Analytical method sensitivities ranged from 0.001 ppm to 0.03 ppm. In the PDP data, there were 27 positive findings of atrazine in wheat out several hundred wheat samples tested each year, and four findings for atrazine in spinach out of a several hundred spinach samples tested. All positive findings in spinach came from New York. These are violative samples as no tolerances for spinach have been established. Most results were at the limit of quantification, but a few results in wheat did range up to 0.03 ppm. All other RACs tested had non-detectable residues for atrazine. PDP did not test samples of sugar cane, field corn, sorghum, guava or macadamia nuts for atrazine.

The FDA monitored for atrazine, parent only, in a wide variety of foods between 1993 through 1998. FDA had six positive findings for atrazine in romaine/iceberg lettuce and endive in 1997. All were from Florida. Results were mostly at the limit of quantification, but did range up to 0.045 ppm atrazine in lettuce. These are violative samples as no tolerances for these commodities have been established. FDA analyzed several hundred samples of each leafy vegetable commodity (romaine, iceberg, endive) each year during this sampling period. These residues may have resulted from rotational crops planted to corn fields after atrazine use. Current plant back intervals are set at 12 months. As quantifiable chlorotriazine residues were detected in soybean forage collected from the 12-month PBI (NY test) limited field trials have been required, as described under OPPTS.GLN 860.1900, to determine appropriate tolerances for inadvertent residues of atrazine in the foliage of legume vegetables. (See Attachment IV.) PDP did not test many samples of sugar cane, field corn, sorghum, wheat, guava or macadamia nuts for atrazine.

FSIS monitored for parent atrazine in the fat of the predominant species of meat animals in 1989 through 1990. FSIS reported finding no detectable residues of atrazine in fat above the currently established tolerance set at 0.02 ppm. Although a method with a sensitivity of 0.005 ppm was used, FSIS only reported finding no samples above the tolerance; but did not report whether there were any positive findings below the tolerances.

Extensive field trials, including recently updated trials reflecting currently labeled use rates, exist for atrazine on corn and sorghum, and adequate field trials also exist on sugar cane and wheat. In these field trials, samples were analyzed for residues of atrazine, each of the three chlorinated metabolites, and each of the four hydroxy-metabolites of atrazine. Old, limited field trials exist for macadamia nuts and guava, in which samples were analyzed for atrazine, per se, only. The guava tolerance is translated from use on other crops. Processing studies are available for processing of sugar cane into refined sugar and molasses. Residue data from the October 18, 1988 Registration Standard Document show residues concentrating in molasses up to 6X and <1X in refined sugar. Because atrazine residues were non-detectable on the sugarcane from this study treated at a 2X rate, a new processing study has been required. A tolerance for sugarcane molasses will be determined from the results of this study. Processing studies are also available for corn, sorghum, and wheat indicating that residues do not concentrate in edible portions of corn, sorghum, and wheat commodities.

Adequate metabolism studies were available for corn, sorghum and sugar cane. Samples from the corn, sorghum and sugarcane studies were analyzed for residues of atrazine, each of the three chlorinated metabolites, and each of the four hydroxy-metabolites of atrazine. Metabolism studies were not available for wheat, guava or macadamia nuts.

Because no reliable field trial data or monitoring data or metabolism data existed for guava, atrazine residues (chloro- and hydroxy-metabolites) were estimated in the exposure assessment based on the established tolerance in guava. Estimates of dietary exposure to atrazine and its chloro- and hydroxy-metabolites based on these assumptions are expected to be conservative and result in overestimations of exposure from guava in the diet.

There were no monitoring data for macadamia nuts, but there were acceptable field trials. All samples from the field trials had non-detectable residues at a limit of detection (LOD) of 0.05 ppm for atrazine and each of the chlorinated metabolites. Residues of atrazine and its chlorinated metabolites in macadamia nuts were estimated in the exposure assessment as the sum of ½ of the LOD for each compound. No metabolism study data were available for macadamia nuts. Neither monitoring nor residue data from field trials were available for the hydroxy-metabolites of atrazine, so the existing tolerance for atrazine in macadamia nuts was used for the dietary assessment for the hydroxy-metabolites. Estimates of dietary exposure to atrazine and its chloro- and hydroxy-metabolites based on these data and assumptions are expected to be conservative and result in overestimations of exposure from macadamia nuts in the diet.

With the exception of a single finding at the LOD for a single hydroxy-metabolite in corn grain in a single field trial, all samples analyzed for atrazine, and its chloro- and hydroxy-metabolites in the corn grain from field trials had non-detectable residues in the edible portions of the crop. All monitoring data showed non-detectable residues of atrazine, but only sweet corn was monitored. Residues of atrazine in field corn have not been monitored by USDA's PDP, FDA or FSIS. Residues of atrazine, and its chloro- and hydroxy-metabolites were found in feed and forage portions of the corn in the field trials. In the exposure assessment, residues in corn grain were estimated from radioactive measurements in the metabolism studies for atrazine and the chlorinated metabolites since the greater sensitivity of these results offered considerable refinement over the field trials. Estimations of the hydroxy-metabolites in corn grain are based on field trials. Estimates of dietary exposure to atrazine, the chloro- and hydroxy-metabolites in edible forms of corn based on these data and assumptions are considered refined, but still conservative.

All field trials showed non-detectable residues of atrazine, and its chloro- and hydroxy-metabolites in sorghum grain. There were no monitoring data for sorghum. To improve refinement, residues for the exposure assessment were estimated from radioactive residues of atrazine, and its chloro- and hydroxy-metabolites detected in sorghum metabolism studies. Estimates of dietary exposure to atrazine, the chloro- and hydroxy-metabolites in edible forms of sorghum based on these data and assumptions are considered refined, but still conservative.

There were no monitoring data for sugar cane. A combination field trial/processing study existed, producing samples with non-detectable residues for atrazine and the chlorinated metabolites in cane sugar and cane molasses. Therefore, a summation of residues at ½ the LODs for atrazine and each chlorinated metabolites was used in the exposure assessment. For the hydroxy-metabolites of atrazine, a value was estimated from a direct measurement in sugar cane molasses from the processing study. No result for the hydroxy-metabolites in refined sugar was available, so a result was extrapolated from the molasses residue, which included information on reduction of residues in refined sugar processed from cane molasses. Estimates of dietary exposure to atrazine, the chloro- and hydroxy-metabolites in edible forms

of sugar based on these data and assumptions are considered refined, but still conservative.

All field trial samples for wheat grain had non-detectable residues of atrazine. PDP did monitor wheat for atrazine, only. Atrazine was found in the monitoring data for wheat grain collected under PDP, and these monitoring data were used in the exposure assessment for wheat. Residues of the chlorinated metabolites in wheat grain were estimated using ratios of atrazine to the chlorinated metabolites from field trials with residue data on wheat forage. For the hydroxyatrazine assessment, the ratio of hydroxy-metabolite residues in wheat forage to parent atrazine in wheat forage was used to convert the residues of parent atrazine found in the PDP monitoring to hydroxy-metabolite residues. Estimates of dietary exposure to atrazine, the chloro- and hydroxy-metabolites in edible portions of wheat based on these data and assumptions are considered refined, but still conservative.

The specific details regarding the calculation and estimation of anticipated residues of atrazine, the chloro- and hydroxy-metabolites in edible portions of crops for use in dietary exposure assessment can be found in Attachment V.

Residue Data for Meat, Milk Poultry, and Eggs:

Residues of atrazine and the chlorinated metabolites may occur in the meat and milk of ruminants as a result of residues present on livestock feeds. These residues could transfer to the human diet through the consumption of meat and milk. As mentioned above, HED's Chemistry Science Assessment Committee determined that residues of atrazine, its chloro- and hydroxy-metabolites were not be expected in tissues of hogs, or in poultry tissues and eggs and could be classified as 180.6(a)3 (memoranda dated 10/5/00 and 10/15/00, C. Eiden, D 269514 & D269608). This decision was based largely on the results of animal feeding studies, in which, residues of atrazine were non-detectable at theoretical dietary burdens. These animal commodities were not included in the dietary exposure assessments.

In 1997 and 1998, PDP tested 1892 samples of milk for atrazine (parent only). All samples had non-detectable residues of atrazine at an average LOD of 0.0075 ppm. Since all samples showed non-detectable residues, more refined estimates were calculated using mass balance estimates using residues found in feed crops and animal feeding studies. Anticipated residues for atrazine and the chlorinated metabolites in meat and milk of ruminants were based on the results of submitted, acceptable animal feeding studies, and reasonable theoretical dietary burdens for beef and dairy cattle. Although not detected in the grains of corn and sorghum, atrazine, the chlorinated metabolites, and the hydroxy-metabolites were detected in animal forages and fodders used for feed. Field trial data were used to calculate anticipated residues in feeds, which were used to estimate the reasonable theoretical dietary burdens for beef and dairy cattle. The reasonable theoretical dietary burdens were used to estimate anticipated residues of atrazine in meat and milk.

The anticipated residue for residues of atrazine and the chlorinated metabolites in milk for chronic dietary exposure assessment was based on residue values from an animal feeding study. Residues in milk at each day of sampling were summed, averaged, and extrapolated to residue values anticipated based on the reasonable theoretical dietary burden for dairy cattle. All samples with non-detectable residues (< 0.01 ppm) were included in the calculation as ½ of the LOD (0.005 ppm).

Anticipated residues for acute dietary assessment of atrazine and the chlorinated metabolites in milk, were based on summing all residues detected of atrazine and the chlorinated metabolites in milk samples taken on a specific day once a plateau in residue values was reached in the study, then averaging the daily values, and extrapolating to residue values anticipated based on the reasonable theoretical dietary burden for dairy cattle. All samples with non-detectable residues were included in the calculation as ½ the LOD (0.005 ppm).

The specific details regarding the calculation and estimation of anticipated residues of atrazine, the chloro- and hydroxy-metabolites in animal tissues and milk for use in dietary exposure assessment can be found in Attachment V.

Percent-Crop-Treated Information:

HED used information on the percentage of crops treated with atrazine supplied by the registrant and contained in OPP's Biological Economic and Analysis Division's (BEAD) Quantitative Usage Analysis (QUA) dated January 2001. BEAD has recently updated percent crop treated information for atrazine. The estimates of usage are considered to be good, estimated with 0.1% precision for the major crops. The estimated percentages of crop-treated used in the dietary assessment were: for sugarcane: 76% (weighted average) to 95% (maximum); for sweet corn: 50% (weighted average) to 60(maximum); for other corn: 75% (weighted average) to 84 % (maximum); for sorghum: 59% (weighted average) to 74% (maximum); and, less than 1% on wheat. BEAD estimated use on macadamia nuts to be approximately 57%. Novartis has suggested that no more than 10% of the guava crop is treated with atrazine, and BEAD has affirmed that this estimate should be conservative. This information on the percentage of the crop treated has been incorporated, as appropriate, into HED's estimates of reasonable theoretical dietary burdens for beef and dairy cattle, and anticipated residues in human foods.

Processing Factors:

While some processing data is available for the sugar cane products, no other cooking or processing information was available for atrazine, and all other processing factors are DEEM^{TM} default factors.

Confined Rotational Crops:

An adequate confined rotational crop study demonstrated that metabolism in rotated crops proceeds via essentially the same pathway as that in primary crops.

Limited field rotational crop studies provided data on residues of atrazine and chloro-metabolites and two hydroxy-metabolites (G-34048 and G-17794) in representative rotational crops (leaf lettuce/spinach, potatoes, wheat, and soybean) planted 5 months (lettuce and wheat only) and 10-12 months following a single postemergence application of the atrazine (4 lb/gal FlC) at 3 lb ai/A/season (1.2x the current maximum seasonal rate and 1.5x the current maximum postemergence rate) to a primary corn crop.

Chlorotriazine residues were non-quantifiable in/on representative rotational crop commodities with few exceptions. Residues of G-28273 were 0.10 ppm in one treated lettuce sample from the 5-month plant-

back interval (PBI). In one wheat trial (5-month PBI; CA) residues of atrazine were 0.06 ppm, and G-30033 residues were 0.06-0.09 ppm in/on two treated fall forage samples; G-28273 residues were 0.06 ppm in/on two treated straw samples. [Although data were not available on wheat from later PBIs, the [^{14}C]atrazine confined study indicated that total chlorotriazine residues may be expected to decline to levels below the method LOQs for wheat forage, grain, and straw at the 9-month PBI.] In addition, two treated soybean forage samples collected from the 11-12 month PBI bore residues of G-28279 and G-30033 at 0.11-0.12 and 0.08-0.09 ppm, respectively.

Residues of both hydroxy-metabolites were <0.02 ppm (<LOQ) in/on treated samples of rotational crops, with the exception of two treated samples of straw (CA test; 5-month PBI) and soybean forage (NY test; 12-month PBI) that each contained residues of GS-17794 at 0.03 ppm.

As the current atrazine EP labels specify a rotational crop restriction of 12 months for rotational crops other than sorghum and corn, tolerances for residues of atrazine in certain rotational crops (small grains, leafy vegetables, and root crops) will not be required. However, as quantifiable chlorotriazine residues were detected in soybean forage collected from the 12-month PBI (NY test) limited field trials are required, as described under OPPTS.GLN 860.1900, to determine appropriate tolerances for inadvertent residues of atrazine in the foliage of legume vegetables.

Dietary Risk Estimates:

These exposure assessments were performed using the Dietary Exposure Evaluation Model (DEEM^{TM}). DEEM^{TM} software was developed by Novigen Sciences, Inc. to perform dietary exposure analyses. DEEM^{TM} software enables the user to match residues found in various foods to the consumption of those foods by the U.S. population and by various subgroups of that population. The food consumption for these populations is taken from USDA's Continuing Survey of Food Intake by Individuals (CSFII), 1989-92 report. When residue data are input into DEEM^{TM}, estimated exposures are reported out both in terms of the absolute exposure (mg/kg/day) and exposure relative to the toxicological endpoint, i.e., as a percentage of the RfD or the population adjusted dose (PAD). Further information on dietary exposure assessment as it is performed by EPA is available at the EPA web site at: www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf. Further information on the DEEM^{TM} program is available at www.epa.gov/scipoly/sap/2000/February/Final_sap_document_Feb_1_2000.pdf.

Acute Dietary Risk Estimate

As previously summarized, acute dietary exposure assessments were conducted for atrazine and its chlorinated metabolites in a refined assessment using anticipated residues based on monitoring data, field trials, metabolism studies, one tolerance level residue for guava, and probabilistic techniques of analysis. As per OPP policy, a reference dose (RfD) modified by a FQPA safety factor is referred to as a population-adjusted dose (PAD). A FQPA safety factor was retained as 10X for atrazine. Therefore, the acute RfD used in the dietary assessment for one-day exposures to atrazine and the chlorinated metabolites was 0.1 mg/kg/day, and the acute population adjusted dose (aPAD) was 0.01 mg/kg/day. For the relevant population subgroup considered under the acute risk assessment, "females (13-50 years old)", the estimated exposure at the 99.9th percentile of exposure is 0.000041 mg/kg body weight/day,

which is <1.0% aPAD. One-day exposures at the 99.9th percentile of exposure that are less than 100% of the aPAD are below HED's level of concern for acute effects. Estimates of risk based on one-day (acute) exposures to atrazine and the chlorinated metabolites for the relevant subgroup is below HED's level of concern. Table 5 shows the results of the acute dietary risk assessment at various percentiles of exposure.

Table 5. Results of the Acute Assessment for Atrazine and its Chlorinated Metabolites

Population Subgroup	Exposure at 95% (mg/kg/day)	Exposure at 95% (%aPAD)	Exposure at 99% (mg/kg/day)	Exposure at 99% (%aPAD)	Exposure at 99.9% (mg/kg/day)	Exposure at 99.9% (%aPAD)
Females 13-50	0.000017	<1.0	0.000025	<1.0	0.000041	<1.0

Milk-based residues were the major contributor to acute exposure to atrazine and the chlorinated metabolites with meat-based residues the second major contributor. Because the residues in these commodities were estimated using the results of the animal feeding studies, the residues in meat and milk are expected to be conservative. Exposure predominates through the transfer of residues to meat and milk foods because atrazine residues occur primarily on the crop parts used as animal feeds, i.e., the stems and leaves of corn and other crops. With the exception of wheat, residues are not found in the grains and nuts treated with atrazine, the crop parts eaten by humans. Residues of atrazine also do not appear to be found in sugar cane or in refined cane sugar. Although a tolerance level residue was used for guava and ½ of the LOD for each compound was used for macadamia nuts, these commodities are insignificant food items in the diet, and have a corresponding insignificant impact on the dietary exposure to atrazine. The dietary exposure model inputs and complete acute analysis are appended to Attachment V.

Chronic Dietary Risk Estimate

As previously summarized, chronic dietary exposure assessments were performed for atrazine and its chlorinated metabolites. As per OPP policy, a reference dose (RfD) modified by an FQPA safety factor is referred to as a population-adjusted dose (PAD). A FQPA safety factor was retained as 10X for atrazine. Therefore, the chronic RfD used in the assessment was 0.018 mg/kg/day, and the chronic population adjusted dose (cPAD) was 0.0018 mg/kg/day. Average exposures less than 100% of the cPAD are below HED's levels of concern for chronic effects. Risk estimates for all subgroups analyzed were less than 1% of the chronic population-adjusted dose (cPAD), and therefore risk estimates for all subgroups are below HED's level of concern. The estimate of chronic dietary exposure and risk for the seven most-highly exposed population subgroups from uses of atrazine on food/feed crops are summarized in Table 6. The dietary exposure model inputs and complete chronic analysis are appended to Attachment V.

Table 6. Results of the Chronic Assessment for Atrazine and its Chlorinated Metabolites

Population Subgroup	Exposure mg/kg/day	Exposure %cPAD
General Population	0.000005	<1.0

Table 6. Results of the Chronic Assessment for Atrazine and its Chlorinated Metabolites		
Population Subgroup	Exposure mg/kg/day	Exposure %cPAD
Infants	0.000008	<1.0
Children 1-6	0.000017	<1.0
Children 7-12	0.000009	<1.0
Females 13-50	0.000003	<1.0
Males 13-19	0.000006	<1.0
Males 20+	0.000003	<1.0
Seniors	0.000003	<1.0

As was the case for acute dietary exposure, the major contributors to chronic exposure to atrazine and the chlorinated metabolites were meat and milk for the aforementioned reasons. Grains eaten by humans, refined sugar, guava and macadamia nuts have an insignificant impact on exposure to atrazine and the chlorinated metabolites in the diet.

In addition, a chronic dietary exposure assessment was performed for the hydroxy-metabolites of atrazine. Available data on exposure to hydroxyatrazine is limited to the oral route. Because the FQPA safety factor was reduced to 1X for the hydroxy-metabolites of atrazine, the chronic RfD for the hydroxyatrazine (0.01 mg/kg/day) is equal to the chronic PAD. All population subgroups had exposures below their respective cPADs. Risk estimates for all subgroups analyzed were less than 1.0% of the chronic population-adjusted dose (cPAD), and therefore risk estimates for all subgroups are below HED's level of concern. "Children, 1 to 6 years old," were the most highly exposed subgroup for chronic exposure assessment for the hydroxy-metabolites at 0.000059 mg/kg/day. The results of the chronic dietary exposure assessment for the hydroxy-metabolites are provided in Table 7.

Table 7. Results of the Chronic Assessment for the Hydroxy-Metabolites of Atrazine		
Population Subgroup	Exposure mg/kg/day	Exposure %cPAD
General Population	0.000025	<1.0
Infants	0.000056	<1.0
Children 1-6	0.000059	<1.0
Children 7-12	0.000045	<1.0
Females 13-50	0.000019	<1.0
Males 13-19	0.000032	<1.0
Males 20+	0.000018	<1.0
Seniors	0.000014	<1.0

As can be seen from these tables, estimated exposures to the hydroxy metabolites of atrazine in food

though minimal are greater than estimated exposures to atrazine and the chlorinated metabolites in food. This is expected as the hydroxy metabolites of atrazine are the dominant plant metabolites of atrazine. For all population subgroups, corn was the major contributor for chronic exposure to the hydroxy-metabolites. The residues estimated on corn are also conservative because ½ LOD value from the field trials was used for each of the two hydroxy metabolites analyzed for in field trial samples of corn grain, rather than the more sensitive metabolism data. Field trial data were used because one of the four hydroxy-metabolites of atrazine was detected above the LOD in one sample of corn in monitoring data collected under the PDP.

Risk Characterization and Sources of Uncertainties:

HED considers the dietary estimates of risk associated with food exposures to be conservative. There was adequate information about atrazine residues in all of the major crops, but it must be noted that only very limited data of any kind was available for guava and macadamia nuts. Virtually all of the information for these latter two crops is uncertain, but neither of these two crops contributes much to overall dietary exposure. Sensitivity analyses showing the effects of removing these two crops from the exposure assessments altogether had almost no effect. There was adequate information to estimate residues in meat and milk using the results of animal feeding studies, but these estimates are expected to be conservative.

The only monitoring data available from PDP or FDA that was used in this assessment was on wheat grain. For the most part, only the parent atrazine has been monitored by FDA or PDP, and there has been sparse monitoring data for all the crops except sweet corn and wheat grain. Where monitoring data existed, no residues were detected except in wheat grain (and in isolated spinach and lettuce samples). (One sample of a cooked chicken breast was also found positive for atrazine at 0.001 ppm in the FDA Total Diet Survey. No other residues of atrazine were found in all of the Total Diet Study sampling over the years 1991 through 1999.)

Because no residues of atrazine were detected on corn or sorghum grain in monitoring or in field trials, residues in corn and sorghum grain could be more accurately estimated from the metabolism studies. Metabolism studies were more accurate because these assays provided much more sensitive estimates of atrazine residues than the monitoring or field trial testing. Even so, these estimates are conservative since the anticipated residue of atrazine and the chlorinated metabolites are less than the total radioactive residues (TRR) measured in the organic extracts from metabolism studies that were used in the dietary assessments.

In 1997 FDA detected illegal residues of atrazine in six lettuce products from Florida: (one endive, one iceberg lettuce and four Romaine lettuce samples) ranging from a trace to 45 ppb. PDP also detected illegal residues of atrazine in 4 spinach samples from New York in 1995-1996. Neither the residues on spinach nor on lettuce contribute significantly to dietary exposure, and these crops were not further investigated in this assessment. Wheat samples collected by PDP also had higher residues of parent atrazine than expected from field trials in slightly more (1.7%) than the 1% expected based on estimates of percent of the wheat crop-treated (1%) by BEAD. The residues on wheat do make a significant contribution to exposure, but HED has no concrete evidence to explain why the residues on wheat are

larger than expected. While wheat is a significant source of exposure, it is not the major contributor to the risk estimates.

Sensitivity analyses were also performed for both assessments of atrazine and it's chlorinated metabolites, and for the chronic assessment for hydroxyatrazine. This was done to estimate the uncertainty from the incorporation of non-detectable residues on crops into the dietary assessment. Setting all non-detectable results were set to zero in these sensitivity analyses impacted the risk estimates insignificantly. The results of these sensitivity analyses can be found in Attachment V (attachments 6.a, 6.b, and 6.c of HED memorandum on "Anticipated Residues and Acute and Chronic Dietary Exposure Assessments for Atrazine", 01/18/01, D. Soderberg & C. Eiden, D272010).

4.2.2 Drinking Water Exposure

Drinking Water Standards:

Atrazine is currently regulated under the Safe Drinking Water Act (SDWA). A Maximum Contaminant Level (MCL) of 3 ppb was established in 1991 by the Agency's Office of Water (OW). The OW has also established a One-Day Health Advisory Level (HAL) of 100 ppb for one-day exposures to atrazine in drinking water.

Environmental Fate and Occurrence:

Atrazine is the most commonly detected pesticide in ground and surface water. It has been the subject of multiple monitoring programs conducted by the registrant, academia, states, and government agencies, in particular the U.S. Geological Survey (USGS). Atrazine's frequent detection in streams, rivers, groundwater, and reservoirs is related directly to both its volume of usage, and its tendency to persist in soils and move with water. Atrazine contamination of surface waters from normal agricultural use occurs through runoff from treated fields, spray drift from fields adjacent to sources of surface water, irrigation, flooding, and unintended atmospheric transport in precipitation. Residues reach groundwater through a slow and steady process of leaching.

Atrazine is metabolized in soil and water to form desethyl atrazine, desisopropyl atrazine, and ultimately the terminal metabolite, diaminochlorotriazine (DACT). DACT has been measured in concentrations equal to atrazine, *per se*, in rural wells, and is believed to be at least as persistent as the parent once formed. The hydroxy metabolites of atrazine are not expected to occur in water in concentrations as significant as the chlorinated metabolites.

Monitoring Data:

There are more monitoring data for atrazine, *per se*, from studies designed to assess ambient water quality, available for assessing the exposure to atrazine in ground and surface water than for any other pesticide. There are also more monitoring data on residues of atrazine in sources of drinking water and finished drinking water than for any other pesticide. The quality of the database for assessing exposures to atrazine and its chlorinated metabolites in drinking water is very high. Typically, in the absence of

appropriate, reliable, and available monitoring data, OPP uses water quality models to provide screening-level estimates of pesticide concentrations in surface water and groundwater. Because monitoring data on atrazine residues in finished drinking water (post-treatment) are available through a variety of monitoring programs, and these data are of high quality, these data were used in the drinking water exposure assessment, instead of OPP's screening-level models.

The databases used in this drinking water exposure assessment for atrazine include: i) compliance monitoring data on atrazine, *per se*, collected under the SDWA for community water systems (CWS) using surface water, groundwater, or blends in 21 major atrazine use states (21,241 CWS), ii) monitoring data on atrazine , *per se*, in subsets of CWS targeted as representing high-end exposures for CWS using surface water (~275 CWS), iii) monitoring data on atrazine and the chlorinated metabolites from a subset of CWS using surface water (17) targeted as having high concentrations of the parent compound, and iv) monitoring data on atrazine, the chlorinated and hydroxylated metabolites in a subset of domestic rural wells (1505) targeted as representing high-end exposures for individuals using rural wells for their drinking water. Data from the 17 CWS (iii) in which atrazine and the chlorinated metabolites were measured was used to estimate the chlorinated metabolites in other CWS using surface water. At the time of this assessment, monitoring data on the chlorinated metabolites in CWS using groundwater of a blend of ground and surface water were not available. These data are being developed by the registrant.

The risk assessments for drinking water exposures to atrazine residues fall into three categories: 1) CWS using surface water, 2) CWS using groundwater or blended water sources, and 3) domestic rural wells in high-use areas for atrazine. The databases listed inder ii), iii), and iv) represent CWS or wells targeted for high-end exposures, only.

(i) Compliance Monitoring Data

Compliance monitoring data under the SDWA have been collected on atrazine, *per se*, for about 10 years. Compliance monitoring data do not include analyses for the chlorinated metabolites of atrazine. The registrant has developed a database that includes all of the compliance monitoring data collected on atrazine under the SDWA from 1993 through 1998 as compiled from state agency monitoring records. This database is called the Population Linked Exposure Database (PLEX) because it cross-links each community water system (CWS) sampled under compliance monitoring with the population it serves. Monitoring data from each CWS located within the 21 states with major atrazine use are included in the database unless a CWS received a monitoring waiver. Monitoring waivers may be granted to a specific CWS if atrazine is not detected after consecutive monitoring across three quarters in a given year, and/or if there is documentation of no atrazine use in areas affecting the CWS. This means there are CWS currently not monitoring for atrazine[1].

The PLEX includes monitoring data from 21,241 CWS, using either surface water (3670 CWS) or groundwater (16,865 CWS) or a blend of both (706), in 21 states with major atrazine use accounting for 92% of all atrazine used in the U.S. These states are: California, Delaware, Florida, Hawaii, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Michigan, Minnesota, Missouri, Nebraska,

[1] Part 2 EPA, 40 CFR Parts 141, 142, 143, Volume 56, No. 20, Wednesday January 30, 1991, pp. 3585-3586, " National Primary Drinking Water Regulations Final Rule".

New York, North Carolina, Ohio, Pennsylvania, Texas, and Wisconsin. This database provides information on the exposure of approximately 166,000,000 people (roughly 59% of the U.S. population) to atrazine residues in their drinking water. The CWS contained in the PLEX database are the CWS expected to have potential impacts resulting from atrazine use. Of these 21,241 CWS monitoring for atrazine from 1993 through 1998, approximately 11% (2386 CWS) had one or more detections of atrazine above limits of quantitation (LOQs) for atrazine. The LOQs used range from 0.01 to 0.5 ppb. Because the SDWA only requires analysis for atrazine, *per se*, this database does not contain residue data on atrazine's chlorinated metabolites. Because PLEX includes those CWS detecting atrazine residues, the Environmental Fate and Effects Division (EFED) has reported the PLEX database to be conservatively biased. At the most, CWS included in the PLEX were sampled once quarterly (4 times per year) as mandated under the SDWA. Because of the infrequency of the sampling, these data may be used reliably to estimate an annual mean concentration of atrazine residues in finished drinking water, but not one-day, short-term, or intermediate-term concentrations over days, weeks or months. Therefore, this database is most useful for developing exposure assessments based on chronic toxic effects. A detailed discussion of the PLEX database can be found in Attachment VII.

(ii) Targeted CWS using Surface Water with High-End Exposures

Based on the results of the compliance monitoring, the registrant initiated a program designed to monitor a subset of those CWS identified in the PLEX database with a history of contamination problems. This targeted monitoring program, which includes CWS on a voluntary basis, is called the Voluntary Monitoring Study (VMS), and has been ongoing since June 1993. Generally, the CWS included in the VMS had exceeded the MCL for atrazine of 3 ppb, or were small reservoirs that drain agricultural watersheds with a history of substantial atrazine use. Consequently, the VMS database is conservatively biased. For CWS included in the program in any given year, finished water samples were collected and analyzed weekly during the months of May, June, and July. Samples were collected biweekly for the remainder of the year. As of 1998, there were 97 CWS included in the VMS. All of the 97 CWS included in the VMS provide drinking water from surface water sources. The registrant analyzed the finished water samples for atrazine, *per se*, and did not include the chlorinated metabolites. Because of the frequency of the sampling, these data may be used reliably to estimate one-day, seasonal and annual mean concentrations of atrazine residues in finished drinking water. Therefore, this database is most useful for developing exposure assessments based on acute, intermediate-term (sub chronic), and chronic effects. Data from all 97 CWS included in the VMS through 1998 were included in this drinking water assessment. A detailed discussion of the VMS database can be found in Attachment VII.

The Aceotochlor Registration Partnership (ARP) was developed as a condition of registration for acetochlor. However, the ARP has also analyzed for atrazine, *per se*. This monitoring program is based on a random, but stratified survey design, in which the largest number of CWS included in the survey represent CWS draining small watersheds with a relatively high percentage of the watershed cropped to corn. The ARP includes 175 CWS in 12 states using surface water as their source. This represents a second targeted monitoring program for CWS using surface water located either in high atrazine use areas or in watersheds with a relatively high percentage of corn agriculture. As in the case of the VMS, the frequency of the sampling in the ARP allows the estimation of peak, seasonal and annual mean concentrations of atrazine residues in finished drinking water. This database is also useful for developing exposure assessments based on both acute, subchronic and chronic effects. A detailed discussion of the ARP database can be found in Attachment VII.

(iii) Targeted CWS Using Surface Water Monitored for Atrazine and the Chlorinated Metabolites

At the request of the Agency, the registrant provided some residue data on the chlorinated metabolites of atrazine in CWS using surface water as their source. Finished drinking water from a subset of 17 CWS included in the VMS, which is also a subset of CWS in the PLEX database, were sampled from August 1997 through July 1998. Samples were collected monthly August through April and biweekly in May, June, and July, and analyzed for atrazine, and each of its chlorinated metabolites: desethyl atrazine, desisopropyl atrazine, and diaminochlorotriazine (DACT). The EFED developed linear regression equations from these data to estimate concentrations of the chlorinated metabolites in the other CWS in the VMS, the PLEX, and the Aceotochlor Registration Partnership (ARP) database. A detailed discussion of the regression approach to estimating concentrations of the chlorinated metabolites in CWS using surface water can be found in Attachment VII. HED notes that data to estimate concentrations of the chlorinated metabolites in CWS using groundwater are being developed, but were not available at this time.

(iv) Rural Wells Targeted for High-End Exposures

The registrant has also provided a database containing residue data on atrazine, its chlorinated metabolites, and its four hydroxy-metabolites for 1505 private, rural drinking water wells in 19 states with major atrazine use called the Rural Well Survey. These wells were sampled during September 1992 to March 1995. These wells were selected in conjunction with the Department of Agriculture for each state included in the survey. The wells were selected based on their proximity to farms growing corn, and general location in atrazine use areas, as well as depth to water. This database represents rural wells targeted for their location in atrazine use areas. Each well was sampled one time only, and analyzed for atrazine, desethyl atrazine (DEA), desisopropyl atrazine (DIA), diaminochloro triazine (DACT), hydroxyatrazine, desethylhydroxyatrazine, desisopropylhydroxyatrazine, and diaminohydroxyatrazine. Because only one sample per well has been taken and analyzed, exposure to atrazine residues in these private rural wells for acute and chronic effects has necessarily been based on a single concentration value. This database is most useful for estimating exposures to that portion of the population that get their drinking water from domestic rural wells located in close proximity to areas of atrazine use.

Monitoring Data Summary

In summary, monitoring data were available to estimate exposures to atrazine and the chlorinated metabolites for two distinct population subgroups: populations served by CWS using surface water in the 21 states with major atrazine use (75,359,918 people), and populations using private rural wells located in atrazine use areas for their drinking water (10% of the population). Monitoring data were available for populations served by CWS using groundwater or blended sources in the 21 states with major atrazine use (73,856,519 people), but estimates of exposure could be made for atrazine, *per se*, only. Monitoring data on the concentrations of the chlorinated metabolites in CWS using groundwater are being collected, but were not available at this time. HED expects to include these data in future revisions to this risk assessment. Additionally, HED has conducted a refined exposure assessment for those populations served by CWS using surface water targeted as having concentrations of atrazine residues considered to represent "high-end" exposures via the VMS and ARP databases.

Monitoring data from all of these databases were used in the exposure assessment for atrazine residues in

drinking water. Data from the PLEX database have been used to estimate national exposures based on peak one-day concentrations and annual average concentrations of atrazine and the chlorinated metabolites. Because the VMS and ARP data represent CWS targeted for high atrazine use and contamination, data from these programs were used to estimate "high-end" exposures for people served by CWS using surface water in atrazine use areas based on the measured maximum one-day to weekly concentrations, annual average concentrations, and seasonal mean concentrations (based on the highest 3-month average concentrations) of atrazine and the chlorinated metabolites in each CWS. Data from the registrant's rural drinking water well survey were used to estimate exposures to atrazine and the chlorinated metabolites of individuals living in areas with high atrazine use and using rural wells adjacent to corn fields.

Exposure Assessment Methodology:

Time-weighted mean concentrations for atrazine and the chlorinated metabolites were calculated and used in the exposure assessment for drinking water. For atrazine alone, the time-weighted annual mean concentrations were calculated for each surface water-sourced CWS in the VMS (by Novarits), ARP (by EFED), and PLEX (by Novarits) databases. The total chloro-triazine (ATZ + DEA + DIA + DACT) annual mean concentrations were calculated by applying the annual regression equation to the time-weighted annual mean atrazine concentrations. For total chloro-triazine, arithmetic seasonal mean concentrations were calculated for each surface water sourced CWS in the VMS and ARP databases. Because the finished drinking water samples were collected weekly (evenly in time) in the VMS across the months of May, June, and July, the need to time-weight these samples prior to calculating a seasonal mean is not necessary. As for ARP, the samples were taken bi-weekly (also evenly in time) for the months from March to August, therefore, it is not necessary to time-weight the seasonal mean concentrations average from May through July from the ARP.

Atrazine and the Chlorinated Metabolites

Exposure and risk estimates have been conducted for each CWS and rural well for which data on atrazine and the chlorinated metabolites were available. HED has estimated risk from exposures to residues of atrazine and the chlorinated metabolites in finished drinking water initially using a deterministic approach under which specific CWS and rural wells with concentrations of residues of atrazine and the chlorinated metabolites above levels of concern are identified. Each CWS identified under the deterministic approach will then be included in a probabilistic assessment that will estimate exposure and risk for the specific population receiving their drinking water from those CWS through the use of distributional data on atrazine residues in drinking water (i.e., different concentrations of atrazine and the chlorinated metabolites in drinking water over time) along with distributions of consumption rates and body weights contained in the USDA's Continuing Survey of Food Intake for Individuals (CSFII). Because of the limited data on each of the rural wells included in the Rural Well Survey (one sample), a probabilistic assessment for each well identified under the deterministic assessment is not possible. This approach was developed to allow for the most efficient use of resources within OPP. Because the sheer volume of available monitoring data is very large, a probabilistic assessment of exposure and risk for populations served by each CWS using all of the data contained in the PLEX, VMS, and ARP databases was prohibitive.

The available monitoring data for atrazine in finished drinking water falls into 3 categories: CWS using surface water, CWS using groundwater, and private rural wells. Data are available for the chlorinated metabolites in rural wells, and are available to estimate the chlorinated metabolites in CWS using surface water, but not for estimating the chlorinated metabolites in CWS using groundwater or blended sources. HED believes it is inappropriate to apply concentrations of the chlorinated metabolites in rural wells to CWS using groundwater, because CWS using groundwater serve a larger number of people (at least 25 people) than individual rural wells, and these CWS typically use deeper sources of groundwater and a larger volume of water than rural wells. There are limited data on the hydroxy-metabolites for rural wells, only.

Deterministic exposure assessments have been conducted for maximum one-day (acute), 3-month seasonal (intermediate-term), and annual average (chronic) exposures to residues of atrazine and the chlorinated metabolites in CWS using surface water, and for one-day, and annual average exposures to residues of atrazine and the chlorinated metabolites in individual rural wells. Because only one concentration value for atrazine and the chlorinated metabolites is available for rural wells, this one value is used in both acute and chronic exposure assessments. For CWS using groundwater, a brief comparison of atrazine concentrations for each CWS to the MCL of 3 ppb has been included.

Under HED's deterministic approach, the maximum measured one-day concentrations of atrazine and the chlorinated metabolites for each CWS using surface water from each database (PLEX, VMS, and ARP) and each well included in the Rural Well Survey have been compared to theoretical concentration limits (based on acute effects) for atrazine and the chlorinated metabolites in drinking water for relevant population subgroups. The theoretical limits for atrazine and the chlorinated metabolites in drinking water based on acute effects are called acute drinking water levels of comparison (acute DWLOCs).

Similarly, a time-weighted annual average concentration of atrazine and the chlorinated metabolites for each CWS using surface water included in each of the databases (PLEX, VMS, and ARP), and a seasonal average concentration (seasonal mean) of atrazine and the chlorinated metabolites for each CWS included in the VMS and ARP were calculated, and compared to theoretical concentration limits (based on the toxic effects identified for atrazine and the chlorinated metabolites resulting from intermediate-term and chronic exposures) for relevant population subgroups. The theoretical limits for atrazine and the chlorinated metabolites in drinking water based on the intermediate-term and chronic effect are called chronic drinking water levels of comparison (chronic DWLOCs). Comparison of seasonal mean concentrations (based on average residues of atrazine and the chlorinated metabolites over 3 months as estimated from the VMS and ARP databases) to chronic DWLOC values is considered appropriate to estimate risk for intermediate-term to chronic effects because the selected effect (the attenuation of the LH surge as a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function in general) occurs between 30 days to 5 months of daily exposure depending on the dose levels used in the animal studies. CWS using surface water with seasonal and/or annual average concentrations of atrazine and the chlorinated metabolites in drinking water greater than chronic DWLOC values have been identified for refined exposure assessment using probabilistic techniques. Wells with combined residues of atrazine greater than chronic DWLOC values have been identified.

A DWLOC value is the portion of the acute PAD or chronic PAD remaining after estimated dietary

(food only) exposures have been subtracted converted to a concentration in ppb. This concentration value represents the available or allowable exposure through drinking water for residues of atrazine and the chlorinated metabolites. Under the acute risk assessment, the remaining portion of the acute PAD is based on dietary exposures at the 99.9th percentile of exposure for each relevant population subgroup considered. Under the chronic risk assessment, the remaining portion of the chronic PAD is based on average dietary exposures for each relevant population subgroup considered. DWLOC values vary for population subgroups depending on dietary exposure through foods for each subgroup, and the assumptions made about drinking water consumption, and body weights for each subgroup.

HED's deterministic assessments for acute exposure to residues of atrazine and the chlorinated metabolites in drinking water assume that all individuals in the assessment receive the same one-day maximum concentration. Deterministic assessments for chronic exposure to residues of atrazine and the chlorinated metabolites in drinking water assume that all individuals in the assessment receive the same seasonal concentration daily over a 3-month period, and the same annual average concentration daily over a one year period. All assessments under the deterministic approach assume that all males drink 2 liters of water per day and weigh 70 kg, all females drink 2 liters of water per day and weigh 60 kg, and all infants and children drink 1 liter of water per day and weigh 10 kg. These consumption and body weight factors are currently used by the OW in setting water quality standards for human health, i.e., MCLs. The OW's Office of Science and Technology (OST) estimates that 90 percent of the population has a per capita ingestion rate of community water (i.e., tap water from municipal supplies) of 2 liters or less per day, and that 90 percent of infants less than one year old and children 1 to 10 years old ingest 1 liter per day or less. They estimate that community water supplies comprise 75 percent of the total water ingested by the U.S. population, where as bottled water comprises 13 percent, and spring, private well or cistern water comprises 10 percent.[2] HED notes that the OW has recently completed its "Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)"[3]. This document recommends using the same consumption rates as given above, and the following body weights for human health exposure assessments: 76 kg for adult males, 67 kg for pregnant females, 30 kg for children 4 to 14 years old, 13 kg for toddlers (1 to 3 years old), and 7 kg for infants (< 1 year old). HED has conducted a separate deterministic risk assessment that includes these newly recommended default values for body weight for comparison.

A CWS identified under the deterministic assessment as having exposures to atrazine residues in excess of DWLOC values will undergo a more refined assessment. A refined assessment using probabilistic techniques is intended to utilize all available data on residue concentrations, specific populations exposed,

---

[2] USEPA, "Estimated Per capita Water Ingestion in the United States, Based on Data Collected by the USDA's 1994-1996 Continuing Survey of Food Intake by individuals", Office of Science and Technology, Office of Water, EPA-822-00-008, April 2000.

[3] U.S. EPA, Office of Water, "Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)". Office of Science and Technology, Office of Water. EPA-822-B-00-004. October 2000, and U.S. EPA Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)". Technical Support Document Volume 1: Risk Assessment. Office of Science and Technology, Office of Water. EPA-822-B-00-005. October

consumption, and body weights for those CWS identified under the deterministic assessment approach. By incorporating the variability inherent in distributions of data effecting individual drinking water exposures into this exposure assessment, the estimates of risk are expected to be the most refined possible and have the least uncertainty.

Hydroxy Metabolites of Atrazine

Exposure assessments have not been conducted for the hydroxy-metabolites of atrazine because of the limited data available, and EFED has determined that although occasional contamination of surface waters by hydroxyatrazine residues cannot be ruled out, in general, hydroxyatrazine is unlikely to contaminate surface water to the same degree as atrazine and some of the chlorinated metabolites. However, HED has compared the lowest chronic DWLOC calculated for hydroxyatrazine (99 ppb) to concentration values expected and/or measured for atrazine's hydroxy metabolites in surface water and groundwater to provide a qualitative estimate of exposure to atrazine's hydroxy metabolites in drinking water.

Risk Estimates for Exposures to Residues of Atrazine and the Chlorinated Metabolites in Drinking Water:

The risk estimates are presented below by drinking water source category. These risk estimates are based on the current default assumptions used by the OW for drinking water consumption and body weights: 2L/70 kg for adult males, 2L/60 kg for adult females, and 1L/10 kg for infants and children.

1) CWS using Surface Water

Risk Estimates for One-Day (Acute) Exposures in CWS using Surface Water

Estimates of acute risk are based on estimates of one-day exposures to residues of atrazine and the chlorinated metabolites in food and drinking water. In this deterministic assessment, HED has estimated acute risk from exposures to residues of atrazine and the chlorinated metabolites in food and drinking water by comparing the maximum measured concentration of atrazine plus an estimation of the chlorinated metabolites in any CWS using surface water from each drinking water monitoring database to the appropriate acute DWLOC value for females 13 to 50 years old. Since the only relevant population subgroup considered under the acute risk assessment is females 13 to 50 years old, the DWLOC value for this subgroup was calculated using the following formula:

$$DWLOC_{acute}\ (\mu g/L) = \frac{[\text{one-day water exposure (mg/kg bw/day)} \times \text{body weight (kg)}]}{[\text{water consumption (L/day)} \times 10^{-3}\ \text{mg/ug}]}$$

$$\text{one-day water exposure (mg/kg bw/day)} = [\text{AcutePAD} - \text{(one-day) food exposure (mg/kg bw/day)}]$$

The acute DWLOC value for females 13 to 50 years old was calculated based on a 99.9th percentile one-day food exposure for this subgroup of 0.000041 mg/kg/day, a 60 kg body weight, a 2L/day drinking water consumption rate, and an acute PAD of 0.01 mg/kg/day. The acute DWLOC value (298 ppb) represents the one-day (maximum) concentration of residues of atrazine and the chlorinated metabolites in drinking water for females 13 to 50 years old that is not expected to result in adverse acute health effects after considering one-day exposures to atrazine residues in food at the 99.9th percentile of exposure. Concentrations of residues of atrazine and the chlorinated metabolites less than 298 ppb do not exceed HED's level of concern for acute effects.

The maximum measured concentrations of atrazine and the chlorinated metabolites detected in each CWS using surface water as contained in the PLEX, the VMS, and the ARP were compared to the acute DWLOC value for females 13 to 50 years old. This comparison can be seen in the figures in Appendix B for the PLEX (Figures B-1 through B-6), Appendix C for the VMS (Figures C-1 through C-6), and Appendix D for the ARP (Figures D-1 through D-3). The figures show the comparison of the maximum concentration of atrazine and the chlorinated metabolites in each CWS for each database to the acute DWLOC value of 298 ppb. Table 8 contains the name of the CWS in each database with the highest one-day concentration, the population served by that CWS, and the year that the maximum concentration occurred. Because all of the one-day maxima from each database are well below the acute DWLOC, HED's level of concern for acute effects from one-day exposures to atrazine and the chlorinated metabolites in drinking water from CWS using surface water is not exceeded. The acute DWLOC (theoretical health-based concentration limit) for atrazine and the chlorinated metabolites is 298 ppb, which is much higher than any maximum concentration measured in any CWS across all of the databases.

Table 8. Community Water Systems (CWS) Using Surface Water with Highest Maximum One-day Concentrations of Atrazine Plus Chlorinated metabolites Compared to Acute DWLOC Value for Females 13 to 50 Years Old.

PLEX Database						
Population Subgroup	Food Exposure @ 99.9th Percentile (mg/kg/day)	acute DWLOC (ppb)	CWS	Maximum Concentration ATZ + CLs (ppb)	Population Served	Population Exposed Above Levels of Concern for Acute Effects
Females (13 to 50 years old)	0.000044	298	Gillespie, IL (1996)	59.8	3900	Zero
Novartis' Voluntary Monitoring Survey (VMS)						

Table 8. Community Water Systems (CWS) Using Surface Water with Highest Maximum One-day Concentrations of Atrazine Plus Chlorinated metabolites Compared to Acute DWLOC Value for Females 13 to 50 Years Old.						
Females (13 to 50 years old)	0.000044	298	Salem, IL (1994)	89	8000	Zero
Acetochlor Registration Partnership (ARP)						
Females (13 to 50 years old)	0.000044	298	Gillespie, IL (1996)	69.1	3900	Zero

Risk Estimates for Intermediate-Term and Chronic Exposures CWS using Surface Water

Estimates of intermediate-term and chronic risk are based on estimates of time-weighted annual average and seasonal exposures to residues of atrazine and the chlorinated metabolites in drinking water coupled with average exposures in food. In this deterministic assessment, HED has estimated intermediate-term and chronic risk from exposures to atrazine residues in food and drinking water by comparing the 3-month (seasonal) average and the annual average concentrations of atrazine and the chlorinated metabolites in any CWS using surface water from each drinking water monitoring database to chronic DWLOC values. Comparison of seasonal mean concentrations (based on an average of atrazine residues over 3 months as estimated from the VMS and ARP databases) to chronic DWLOC values is considered appropriate to estimate risk for intermediate-term to chronic effects because the chronic effect (the attenuation of the LH surge as a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function in general) occurs between 30 days to 5 months of daily exposure depending on the dose levels used in the animal studies. Chronic DWLOC values for relevant population subgroups considered under the chronic risk assessment were calculated using the following formula:

$$DWLOC_{chronic}(ug/L) = \frac{chronic\ water\ exposure\ (mg/kg\ bw/day) \times body\ weight\ (kg)}{water\ consumption\ (L/day) \times 10^{-3}\ mg/ug}$$

nic water exposure (mg/kg/day) = [Chronic PAD – (average food + chronic residential exposure (ADE)) (mg/kg/

The chronic DWLOC values for each population subgroup of interest are provided in Table 9. As shown, DWLOC values vary with assumptions about body weights and drinking water consumption rates for each population subgroup. The chronic DWLOC values range from 18 ppb for infants and children's subgroups to 63 ppb for adult male subgroups and 54 ppb for adult female subgroups. These chronic DWLOC values reflect OW's current default assumptions about average body weights for each population subgroup. [Note: There are no anticipated intermediate-term or chronic residential exposures to atrazine.]

Table 9. Chronic DWLOC Values for Comparison to Average Annual and Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Detected in Drinking Water (ppb)		
Population Subgroup	Average Food Exposure (mg/kg/day)	Chronic DWLOC (ppb)
General Population	0.000005	63
Infants	0.000008	18
Children 1-6	0.000017	18
Children 7-12	0.000009	18
Females 13-50	0.000003	54
Males 13-19	0.000006	63
Males 20+	0.000003	63
Seniors	0.000003	63

* DWLOC values are based on current OW default assumptions about body weights.

The calculated chronic DWLOC values represent the average concentration of residues of atrazine and the chlorinated metabolites in drinking water that is not expected to result in adverse chronic health effects after considering long-term, average exposures to atrazine residues in food for each population subgroup of interest. Time-weighted annual averages used in this assessment were calculated for each CWS using surface water for each year that the CWS was included in the PLEX, VMS, and ARP databases. The seasonal mean concentrations were calculated based on weekly concentrations from May through July and calculated for each CWS for each year that the CWS was included in the VMS database, and biweekly concentrations from May through July and calculated for each CWS for each year that the CWS was included in the ARP database. Seasonal mean concentrations were not calculated for CWS in the PLEX database, because of the infrequency of sampling and the availability of richer databases with more frequent monitoring, i.e., the VMS and ARP programs.

The time-weighted annual average concentration of atrazine and the chlorinated metabolites detected in each CWS contained in the PLEX, the VMS, and the ARP were compared to the chronic DWLOC values presented in Table 9. This comparison can be seen in the figures in Appendix B for the PLEX (Figures B-7 through B-12), Appendix C for the VMS (Figures C-7 through C-11), and Appendix D for the ARP (Figures D-4 through D-6). Table 10 contains the name of the CWS in each database with an annual average concentration approaching, equal to, or greater than 18 ppb, the population served by that CWS, and the year that the highest annual average concentration occurred. All of the CWS in the PLEX database had average annual concentrations of atrazine and the chlorinated metabolites below the chronic DWLOC values. The highest annual average concentration of atrazine and the chlorinated metabolites in any CWS in the PLEX database was 17 ppb. Two CWS, Shipman and Hettick both in Illinois, included in the VMS had annual average concentrations of atrazine and the chlorinated metabolites greater than 18 ppb. These annual average concentrations in excess of 18 ppb occurred in 1996. For any given year from 1993 to 1998, all other CWS included in the VMS had average annual concentrations less than 18 ppb. One CWS included in the ARP had an annual average concentration greater than 18 ppb, which occurred in 1996. For any given year from 1995 to 1997, all other CWS included in the ARP had average annual concentrations less than 18 ppb. CWS with the notation “self” in

the Comment column of Table 10, supply water to immediate residents, only. CWS with the notation "self/supplier" in the Comment column of Table 10, supply water to immediate residents and sell water to purchasers as noted. These results are summarized in Table 10.

Table 10. Community Water Systems (CWS) using Surface Water with Highest Time-Weighted Average Annual Concentrations of Atrazine Plus Chlorinated metabolites for Comparison to Chronic DWLOC Values*.

VMS Database					
Year	CWS	Annual Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
1996	Shipman, IL	18.9	675**	18	self ***
1996	Hettick, IL	18.6	250	18	self
Acetochlor Registration Partnership (ARP)					
1996	Shipman, IL	17.6	675**	18	self

* DWLOC values are based on current OW default assumptions about body weights. ** Reported as 365 to 675 people served.
*** Supplies drinking water to population served by that CWS only.

The CWS serving Shipman, IL was included in the VMS program from 1993 through 1998; it was also included in the ARP program from 1995 through 1997. This CWS exceeded an annual mean concentration of 18 ppb in 1996 only, as identified in both the VMS and ARP monitoring programs. The CWS serving Shipman, IL had annual average concentrations below 18 ppb in all other years for which monitoring data were available. The CWS serving Hettick, IL was included in the VMS program from 1993 through 1998; it was not included in the ARP program. This CWS exceeded an annual mean concentration of 18 ppb in 1996 only, as identified in the VMS program. Hettick, IL had annual average concentrations below 18 ppb in all other years for which monitoring data were available. HED notes that the Shipman reservoir (serving 650 people) no longer serves as a drinking water source; in 1999 the town of Shipman was switched to an alternative source of drinking water.

The VMS and ARP programs sampled CWS using surface water with much greater frequency than the PLEX. Seasonal mean concentrations were calculated based on concentrations detected from May to July for each CWS for each year it was included in either the VMS or ARP. For the CWS included in the VMS, these seasonal mean concentrations were based on weekly sampling during May, June, and July, and for the ARP the seasonal mean concentrations were based on biweekly sampling during these same months. These months were chosen as the basis of the seasonal means, because residues of atrazine are known to be at their highest in surface water during this period as it reflects recent applications of atrazine, and the effects of Spring rainfall on concentrations in streams and rivers that feed surface water sources of drinking water. These seasonal mean concentrations were estimated for atrazine and the chlorinated metabolites and compared to chronic DWLOC values. This comparison can be seen in the figures in Appendix C for the VMS (Figures C-12 through C-16), and Appendix D for the ARP (Figures D-7 through D-9). The CWS in the VMS and ARP with a seasonal mean concentrations approaching, equal to, or greater than 18 ppb are provided below in Table 11. CWS with the notation

"self" in the Comment column of Table 11, supply water to immediate residents, only. CWS with the notation "self/supplier" in the Comment column of Table 11, supply water to immediate residents and sell water to purchasers as noted.

Table 11. Community Water Systems (CWS) using Surface Water with Highest Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Compared to Chronic DWLOC Values.

VMS Database

Year	CWS	Seasonal Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
1998	Hettick, IL	19.27	250	18	self
1996	Shipman, IL	39.1	675	18	self
1996	Hettick, IL	32.86	250	18	self
1994	Salem, IL	42.45	8000	18	self
1994	Palmyra-Modesto water Co., IL	21.92	60	18	self/supplier
1994	Palmyra, IL	21.92	850	18	purchased water from Palmyra-Modesto Co.
1994	Modesto, IL	21.92	240	18	purchased water from Palmyra-Modesto Co.
1994	Scottsville Rural Water Co., IL	21.92	510	18	purchased water from Palmyra-Modesto Co.
1994	Hillsboro, IL	19.27	4400	18	self/supplier
1994	Coffeen, IL	19.27	736	18	purchased water from Hillsboro
1994	Schram City, IL	19.27	700	18	purchased water from Hillsboro
1994	Taylor Springs, IL	19.27	650	18	purchased water from Hillsboro
1993	Salem, IL	61.61	8000	18	self
1993	Farina, IL	24.79	600	18	self
1993	Kinmundy, IL	24.79	940	18	self
1993	Shipman, IL	24.79	675	18	self

Table 11. Community Water Systems (CWS) using Surface Water with Highest Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Compared to Chronic DWLOC Values.					
VMS Database					
Year	CWS	Seasonal Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
1993	ADGPTV, IL	20.85	1257	18	self/supplier
1993	Girard, IL	20.85	2400	18	purchased water from ADGPTV
1993	Nilwood	20.85	1063	18	purchased water from ADGPTV
1993	Virden	20.85	3650	18	purchased water from ADGPTV
1993	Auburn	20.85	3724	18	purchased water from ADGPTV
1993	Divernon	20.85	1200	18	purchased water from ADGPTV
1993	Pawnee	20.85	2384	18	purchased water from ADGPTV
1993	Thayer	20.85	830	18	purchased water from ADGPTV
1993	Palmyra-Modesto water Co., IL	19.52	60	18	self/supplier
1993	Palmyra, IL	19.52	850	18	purchased water from Palmyra-Modesto Co.
1993	Modesto, IL	19.52	240	18	purchased water from Palmyra-Modesto Co.
1993	Scottsville Rural Water Co., IL	19.52	510	18	purchased water from Palmyra-Modesto Co.
Acetochlor Registration Partnership (ARP)					
1996	Shipman, IL	33.86	675	18	self
1996	Gillespie, IL	32.17	3900	18	self/supplier
1996	Kaho Water District, IL	32.17	847	18	Purchased water from Gillespie

Table 11. Community Water Systems (CWS) using Surface Water with Highest Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Compared to Chronic DWLOC Values.					
VMS Database					
Year	CWS	Seasonal Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
1996	Benld, IL	32.17	1634	18	Purchased water from Gillespie
1996	Dorchester, IL	32.17	531	18	Purchased water from Gillespie
1996	Eagerville, IL	32.17	127	18	Purchased water from Gillespie
1996	Mount Clare, IL	32.17	297	18	Purchased water from Gillespie
1996	Wilsonville, IL	32.17	609	18	Purchased water from Gillespie
1996	Spring Ck Water Assn., IL	32.17	60	18	Purchased water from Gillespie
1996	Scottsburg, IN	22.95	5500	18	self
1995	Holland, IN	21.15	895	18	self

* DWLOC values are based on current OW default assumptions about body weights.

There are 11 CWS that had seasonal mean concentrations approaching, equal to, or greater than 18 ppb between 1993 and 1998. These 11 CWS represent 0.05% of the 21,241 CWS included in the PLEX database. These 11 CWS serve a population of approximately 26,500 people. Four of these CWS had seasonal mean concentrations greater than 18 ppb in 2 out of the 6 years for which monitoring data were available; Shipman, Hettick, Salem, and Palmyra-Modesto Water Co. These are the same four CWS with annual average concentrations of atrazine residues greater than 18 ppb identified above in Table 9. Nine of these CWS are located in Illinois, and 2 in Indiana. Of the 9 CWS located in Illinois, 4 sold water during the period of 1993 to 1998 to 20 adjacent towns/cities serving an additional 23,000 people. Based on seasonal mean concentrations of atrazine residues in 11 CWS, approximately 49,500 people are known to have been exposed to average seasonal concentrations in excess of 18 ppb in at least one season during the period 1993 to 1998. Risk estimates for these 11 CWS exceed HED's level of concern for infants and children, only. The U.S. Bureau of Census estimates that children 5 years old and under comprise 6.87% of the U.S. population.

One CWS had seasonal mean concentrations of 62 ppb in 1993. This is the maximum seasonal mean concentration measured at any CWS in the available databases. Risk estimates for this CWS in Salem, IL exceed HED's level of concern for adult females as well as infants and children. All other CWS during the period of monitoring from 1993 to 1998, had seasonal mean concentrations at levels that did

not exceed HED's level of concern for any adult (male and female) population subgroup.

The 11 CWS identified for refined probabilistic assessment are: Hettick, Shipman, Salem, Palmyra-Modesto, Hillsboro, Farina, Kinmundy, ADGPTV, and Gillespie in Illinois, Holland and Scottsburg in Indiana. Distributions of residue data for each of these CWS is available from the VMS and/or ARP databases for use in a refined probabilistic assessment. HED notes that the Shipman reservoir (serving 650 people) no longer serves as a drinking water source; in 1999 the town of Shipman was switched to an alternative source of drinking water.

The results of a separate deterministic risk assessment using recommendations from the OW's final report, "Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)", have been included for consideration. This document recommends using the following daily drinking water consumption rate and body weights for human health exposure assessments for these population subgroups: 2L/76 kg for adult males, 2L/76 kg for adult females, 2L/67 kg for pregnant females, 1L/30 kg for children 4 to 14 years old, 1L/13 kg for toddlers (1 to 3 years old), and 1L/7 kg for infants (< 1 year old). Acute and chronic DWLOC values for the relevant population subgroups considered under acute and chronic risk assessments are provided in Table 12.

Table 12. Acute and Chronic DWLOC Values Using OW's Newly Recommended Body Weights for Comparison to Average Annual and Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Detected in Drinking Water (ppb)

Population Subgroup	Food Exposure @ 99.9th Percentile	Average Food Exposure (mg/kg/day)	Acute DWLOC (ppb)	Chronic DWLOC (ppb)*
General Population	N/A	0.000005	N/A	68
Infants	N/A	0.000008	N/A	12.5
Children 1-6	N/A	0.000017	N/A	23
Children 7-12	N/A	0.000009	N/A	53
Females 13-50	0.000044	0.000003	333	60
Males 13-19	N/A	0.000006	N/A	68
Males 20+	N/A	0.000003	N/A	68
Seniors	N/A	0.000003	N/A	68

* DWLOC values are based on OW's newly recommended default assumptions about body weights. "Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)".

The newly recommended defaults for body weights affect the DWLOC values as shown. For all population subgroups, except infants (< 1 year old), DWLOC values increase as a result of increased body weights. The acute DWLOC for the relevant subgroup considered under the acute risk assessment is 333 ppb for females 13 to 50 years old. This DWLOC value is much greater than any measured one-day maxima detected in any CWS or rural well contained in the PLEX, VMS, ARP, and Rural Well Survey as shown previously in Table 8. As a result, HED's level of concern for acute effects resulting from of one-day maximum exposures to atrazine and the chlorinated metabolites under either of the deterministic approaches used to estimate acute risk is not exceeded.

The lowest chronic DWLOC value for comparison to time-weighted average annual and seasonal mean concentrations in finished drinking water is 12.5 ppb for infants (< 1 year old). The results of a comparison of this DWLOC (12.5 ppb) to time-weighted average annual and seasonal mean concentrations of atrazine and the chlorinated metabolites from the PLEX, VMS, and ARP are provided in Tables 13 and 14. CWS with the notation "self" in the Comment column of Tables 13 and 14, supply water to immediate residents, only. CWS with the notation "self/supplier" in the Comment column of Tables 13 and 14, supply water to immediate residents and sell water to purchasers as noted.

Table 13. Community Water Systems (CWS) using Surface Water with Highest Time-Weighted Average Annual Concentrations of Atrazine Plus Chlorinated metabolites for Comparison to Chronic DWLOC Values.

Year	CWS	Annual Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
PLEX Database					
1996	Sardinia, OH	14.98	940	12.5	self
1996	Shipman, IL	13.07	675	12.5	self
1996	Hettick, IL	12.33	220	12.5	self
1996	Gillespie, IL	11.80	3900	12.5	self/supplier**
1994	Drexel, MO	16.97	936	12.5	self
1994	Dearborn, MO	14.33	600	12.5	self
1994	Hillsboro, IL	12.15	4400	12.5	self/supplier**
1994	Palmyra-Modesto	11.65	60	12.5	self/supplier**
VMS Database					
1996	Shipman, IL	18.9	675	12.5	self
1996	Hettick, IL	18.6	250	12.5	self
1996	Carlinville, IL	11.8	6688	12.5	
1994	Salem, IL	13.1	8000	12.5	self
1994	Palmyra-Modesto, IL	13.5	60	12.5	self/supplier
Acetochlor Registration Partnership (ARP)					
1996	Shipman, IL	17.6	365	12.5	self
1996	Gillespie, IL	11.0	7000	12.5	self/supplier

* DWLOC values are based on OW's newly recommended default assumptions about body weights. "Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)". ** These CWS sell water to other CWS. See tables 10 and 13 for CWS purchasing water from Palmyra-Modesto and Gillespie.

Under this approach to the deterministic assessment, 10 CWS using surface water (8 in addition to the

2 CWS identified above in Table 10) were identified for probabilistic assessment based on a comparison of average annual concentrations approaching, equal to, or greater than a chronic DWLOC value of 12.5 ppb. These CWS are: Sardinia (OH), Shipman (IL), Hettick (IL), Carlinville (IL), Salem (IL), Palmyra-Modesto (IL), Gillespie (IL), Drexel (MO), Dearborn (MO), and Hillsboro (IL). The CWS at Gillespie, IL sold water in 1996 to several other towns/cities in Illinois: Kaho Public Water District (serving 847 people), Benld (serving 1634 people), Dorchester (serving 531 people), Eagerville (serving 127 people), Mount Clare (serving 297 people), Wilsonville (serving 609 people), and Spring Creek Water Association (serving 60 people). The CWS at Gillespie had time-weighted annual average concentrations of atrazine and the chlorinated metabolites approaching 12.5 ppb, but not in excess of 11.0 ppb. The CWS at Hillsboro, IL sold water in 1994 to several towns/cities in Illinois: Coffeen (serving 736 people), Schram City (serving 700 people), and Taylor Springs (serving 650 people). The CWS at Palmyra-Modesto, IL sold water in 1994 to several towns/cities in Illinois: Palmyra (serving 850 people), Modesto (serving 240 people), and Scottsville Rural Water Co. (serving 510 people). HED notes that the Shipman reservoir (serving approximately 650 people) no longer serves as a drinking water source; in 1999 the town of Shipman was switched to an alternative source of drinking water.

Table 14 shows the results of the comparison of a 12.5 ppb chronic DWLOC value to seasonal mean concentrations from CWS included in the VMS and ARP approaching, equal to, or greater than 12.5 ppb. [Note: The seasonal mean concentrations for CWS sampled in Illinois in 1993 under the VMS program are based on one sample in June and weekly samples in July, only. The VMS program was not initiated until June of 1993, therefore, weekly samples in May and a portion of June of 1993 were not available to estimate seasonal concentrations.]

Table 14. Community Water Systems (CWS) using Surface Water with Highest Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Compared to Chronic DWLOC Values.

VMS Database					
Year	CWS	Seasonal Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
1998	Hettick, IL	19.27	250	12.5	self
1998	Chariton, IA	12.0	4616	12.5	self
1997	Iberville, LA	16.83	10,400	12.5	self
1997	Bucklin, MO	15.71	616	12.5	self
1996	Shipman, IL	39.1	675	12.5	self
1996	Hettick, IL	32.86	250	12.5	self
1996	White Hall, IL	17.51	2950	12.5	
1996	Centralia, IL	17.28	14,274	12.5	
1994	Salem, IL	42.45	8000	12.5	self
1994	Palmyra-Modesto water Co., IL	21.92	60	12.5	self/supplier

Table 14. Community Water Systems (CWS) using Surface Water with Highest Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Compared to Chronic DWLOC Values.					
VMS Database					
Year	CWS	Seasonal Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
1994	Palmyra, IL	21.92	850	12.5	purchased water from Palmyra-Modesto Co.
1994	Modesto, IL	21.92	240	12.5	purchased water from Palmyra-Modesto Co.
1994	Scottsville Rural Water Co., IL	21.92	510	12.5	purchased water from Palmyra-Modesto Co.
1994	Hillsboro, IL	19.27	4400	12.5	self/supplier
1994	Coffeen, IL	19.27	736	12.5	purchased water from Hillsboro
1994	Schram City, IL	19.27	700	12.5	purchased water from Hillsboro
1994	Taylor Springs, IL	19.27	650	12.5	purchased water from Hillsboro
1994	Hettick, IL	16.50	250	12.5	self
1994	Shipman, IL	13.09	675	12.5	self
1994	ADGPTV	11.66	1183	12.5	self/supplier
1993	Salem, IL	61.61	8000	12.5	self
1993	Farina, IL	24.79	600	12.5	self
1993	Kinmundy, IL	24.79	940	12.5	self
1993	Shipman, IL	24.79	675	12.5	self
1993	ADGPTV, IL	20.85	1257	12.5	self/supplier
1993	Girard, IL	20.85	2400	12.5	purchased water from ADGPTV
1993	Nilwood	20.85	1063	12.5	purchased water from ADGPTV
1993	Virden	20.85	3650	12.5	purchased water from ADGPTV
1993	Auburn	20.85	3724	12.5	purchased water from ADGPTV
1993	Divernon	20.85	1200	12.5	purchased water from ADGPTV
1993	Pawnee	20.85	2384	12.5	purchased water from ADGPTV

Table 14. Community Water Systems (CWS) using Surface Water with Highest Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Compared to Chronic DWLOC Values.					
VMS Database					
Year	CWS	Seasonal Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
1993	Thayer	20.85	830	12.5	purchased water from ADGPTV
1993	Palmyra-Modesto water Co., IL	19.52	60	12.5	self/supplier
1993	Palmyra, IL	19.52	850	12.5	purchased water from Palmyra-Modesto Co.
1993	Modesto, IL	19.52	240	12.5	purchased water from Palmyra-Modesto Co.
1993	Scottsville Rural Water Co., IL	19.52	510	12.5	purchased water from Palmyra-Modesto Co.
1993	Wayne City, IL	16.91	1424	12.5	self
Acetochlor Registration Partnership (ARP)					
1997	Batesville, IN	14.67	6500	12.5	
1996	Shipman, IL	33.86	675	12.5	self
1996	Gillespie, IL	32.17	3900	12.5	self/supplier
1996	Kaho Water District, IL	32.17	847	12.5	Purchased water from Gillespie
1996	Benld, IL	32.17	1634	12.5	Purchased water from Gillespie
1996	Dorchester, IL	32.17	531	12.5	Purchased water from Gillespie
1996	Eagerville, IL	32.17	127	12.5	Purchased water from Gillespie
1996	Mount Clare, IL	32.17	297	12.5	Purchased water from Gillespie
1996	Wilsonville, IL	32.17	609	12.5	Purchased water from Gillespie
1996	Spring Ck Water Assn., IL	32.17	60	12.5	Purchased water from Gillespie
1996	Scottsburg, IN	22.95	5500	12.5	
1996	Vandalia, MO	17.10	3000	12.5	

Table 14. Community Water Systems (CWS) using Surface Water with Highest Seasonal Mean Concentrations of Atrazine Plus Chlorinated metabolites Compared to Chronic DWLOC Values.					
VMS Database					
Year	CWS	Seasonal Average Concentration ATZ + CLs (ppb)	Population Served	Lowest Chronic DWLOC (ppb)	Comment
1996	White Hall, IL	16.40	2900	12.5	
1996	Flora, IL	12.29	6630	12.5	self
1996	Sorento, IL	11.94	6500	12.5	self
1995	Holland, IN	21.15	895	12.5	
1995	West Salem, IL	17.26	1120	12.5	
1995	North Vernon, IN	12.74	9056	12.5	
1995	Carlinville, IL	12.28	8000	12.5	self

* DWLOC values are based on OW's newly recommended default assumptions about body weights. "Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000)".

Under this approach to the deterministic assessment 24 CWS using surface water (13 in addition to the 11 CWS identified above in Table 11) were identified for probabilistic assessment based on a comparison of average annual concentrations of atrazine and the chlorinated metabolites to a chronic DWLOC value of 12.5 ppb. These CWS are: Gillespie, Hettick, Shipman, Salem, Palmyra-Modesto, Hillsboro, Farina, Kinmundy, ADGPTV, Carlinville, West Salem, Flora, Sorento, Chariton, Iberville, White Hall, Centralia, and Wayne City in Illinois, Batesville, Holland, North Vernon, and Scottsburg in Indiana, and Bucklin, and Vandalia in Missouri. Distributions of residue data for each of these CWS is available from the VMS and/or ARP databases for use in a refined probabilistic assessment. The CWS at Gillespie, Palmyra-Modesto, Hillsboro, and ADGPTV selling drinking water to purchasers as seen in Table 14. Drinking water from these 24 CWS is believed to serve approximately 130,000 people .

HED notes that the Shipman reservoir (serving 650 people) no longer serves as a drinking water source; in 1999 the town of Shipman was switched to an alternative source of drinking water. The drinking water source at White Hall was switched from surface water to groundwater in 1997.

These 24 CWS are monitored under the SDWA for atrazine. These 24 CWS represent variously 0.11% of all CWS monitored under the SDWA using either surface or groundwater or a blend, 0.5% of the 4886 CWS using surface water, and 0.65% of the 3670 CWS using surface water with data on atrazine residues. Under this deterministic assessment, these 24 CWS have been identified for probabilistic risk assessment. Probabilistic assessments using all available distributional data on drinking water residues, body weights, and drinking water consumption would reduce the uncertainty associated with these risks, which have been estimated deterministically.

Rural Wells

Acute and Chronic Risk Estimates for Rural Wells.

Because only one well concentration was available for each rural well sampled, this concentration value was used as an estimate of maximum and average concentrations of atrazine residues in each rural well. The highest measured concentration from any well in the Rural Well Survey was 18 ppb. For individuals using private rural wells, HED has no concern for acute effects as a result of one-day maximum exposures to atrazine and the chlorinated metabolites under either of the deterministic approaches used to estimate acute risk. For adults, there are no concerns for chronic exposures to atrazine residues in rural wells under either of the deterministic approaches used to estimate chronic risk. Based on the newly recommended average body weights for infants (< 1 year old) 8 rural wells out of the 1505 sampled once had concentrations of atrazine and the chlorinated metabolites of 12.5 ppb or greater, there are some concerns for chronic exposures of infants using private rural wells in close proximity to atrazine use areas.

CWS using Groundwater or Blended Water

Acute and Chronic Risk Estimates for CWS using Groundwater.

A partial risk assessment was conducted using the available monitoring data in the PLEX database on residues of atrazine, per se, in finished drinking water from CWS using groundwater. Data to estimate concentrations of the chlorinated metabolites in CWS using groundwater are still being developed, and were not available at this time. For the portion of the U.S. population receiving their drinking water from CWS using groundwater as the source (73,856,519 people), HED notes that 95.6% of this population are served by CWS with no detections of atrazine residues in finished drinking water. Four percent (4%) of this population received drinking water with quarterly concentrations of atrazine, per se, that were less than 3 ppb, and 0.4% of this population received quarterly concentrations of atrazine, per se, greater than 3 ppb, and 0.004% of this population (3000 people) received annual average concentrations greater than 3 ppb. None of the CWS using groundwater in PLEX were targeted for inclusion in the VMS program. Although the risk assessment is incomplete without an estimate of the chlorinated metabolites in each CWS, the preliminary indication is that CWS using groundwater are not impacted as heavily by atrazine use as CWS using surface water. However, HED reserves its preliminary risk estimate for CWS using groundwater until the data for estimating concentrations of the chlorinated metabolites in CWS using groundwater is available, and this risk assessment can be completed.

Risk Estimates for Atrazine's Hydroxy Metabolites in Drinking Water:

Exposure assessments have not been conducted for the hydroxy-metabolites of atrazine because of the limited data available, and EFED has determined that although occasional contamination of surface waters by hydroxyatrazine residues cannot be ruled out, in general, hydroxyatrazine is unlikely to contaminate surface water to the same degree as atrazine and some of the chlorinated metabolites. HED notes that the lowest chronic DWLOC for hydroxyatrazine is 99 ppb (based on current OW default values defaults for body weight for children and infants of 10 kg) or 69 ppb (based on a default body weight of 7 kg for infants less than 1 year old). As average annual concentrations of hydroxyatrazine are not expected to

exceed those of atrazine and the chlorinated metabolites in surface water, it is unlikely that average annual concentrations of the hydroxyatrazine residues would exceed 20 ppb (the maximum measured time-weighted annual average concentration for atrazine and the chlorinated metabolites in a CWS using surface water) as seen in Table 10. Therefore, HED does not expect average annual concentrations of the hydroxy-metabolites in finished drinking water from CWS using surface water to exceed the lowest chronic DWLOC for chronic effects of 99 ppb. This is the concentration of the hydroxy metabolites of atrazine in drinking water that are not expected to result in adverse health effects for children once average exposures to the hydroxy metablites in food are considered. As the highest concentration of hydroxy-metabolites in rural wells was 7.66 ppb, HED does not expect concentrations of the hydroxy-metabolites in finished drinking water from CWS using groundwater or in private rural wells to be of concern. Based on the chronic DWLOC for hydroxyatrazine, and available but limited data, exposures to hydroxy-metabolites in finished drinking water are expected to be an insignificant contributor of risk.

Risk Characterization and Sources of Uncertainty:

Atrazine and the Chlorinated Metabolites

Because people receive their drinking water from various sources, i.e., CWS using either surface water, groundwater, or a blend, and private rural wells, and the estimated risks associated with exposure to atrazine residues in drinking water are presented by drinking water source, the following uncertainty discussion is by drinking water source category, as well. Overall, the risk estimates presented in this document are considered to be conservative. There is uncertainty associated with the deterministic approach used in estimating these risks. In particular, the use of two different sets of default assumptions about average body weights in the deterministic exposure assessment emphasizes the importance of using all available distributional data on atrazine residues, body weight, and consumption in a probabilistic assessment to estimate chronic exposures to atrazine residues in those CWS identified under the deterministic approach as having drinking water exposures exceeding HED's level of concern. Probabilistic assessments of these CWS will refine the risk estimates.

For the portion of the U.S. population living in states accounting for 92% of atrazine use (75,359,918 people) receiving their drinking water from 4886 CWS using surface water, HED's level of concern for acute exposures to residues of atrazine and the chlorinated metabolites in drinking water (based on maximum measured concentrations) for any relevant population subgroup is not exceeded. HED's level of concern is not exceeded for chronic exposures (based on time-weighted annual average concentrations) to atrazine residues in drinking water for any of the subgroups categorized as adult males and adult females. One CWS had seasonal mean concentrations of 62 ppb in 1993. This is the maximum seasonal mean concentration measured at any CWS in the available databases. Risk estimates for this CWS in Salem, IL exceeded HED’s level of concern for adult females as well as infants and children in 1993. All other CWS during the period of monitoring from 1993 to 1998, had seasonal mean concentrations at levels that did not exceed HED’s level of concern for any adult (male and female) population subgroup. Risk estimates based on seasonal mean concentrations values exceeded HED’s level of concern for infants and children receiving their drinking water either directly or as purchased water from any of the 24 CWS identified as: Gillespie, Hettick, Shipman, Salem, Palmyra-Modesto, Hillsboro, Farina, Kinmundy, ADGPTV, Carlinville, West Salem, Flora, Sorento, White Hall, Centralia, and Wayne City in Illinois, Chariton in Iowa, Batesville, Holland, North Vernon, and Scottsburg in Indiana, Iberville in Louisiana, and

Bucklin, and Vandalia in Missouri.

HED believes the risk estimates for annual, seasonal, and maximum one-day exposures to residues of atrazine and the chlorinated metabolites are conservative for that portion of the population receiving their drinking water from CWS using surface water, because these exposures and risks have been estimated using a deterministic approach, in which, a single residue value, a point estimate of either a maximum value for acute effects or an average value for chronic effects, is assumed along with 90th percentile default drinking water consumption rates, and average body weights for individuals in each population subgroup considered in the assessment. A probabilistic assessment using all available data on atrazine residues in drinking water, consumption, and body weights in a distributional analysis would provide more accurate estimates of risk.

HED further believes the risk estimates based on seasonal pulses of residues of atrazine and the chlorinated metabolites to be conservative because atrazine attenuation of the LH surge is time and dose dependent; lower doses of atrazine require longer periods of time to produce an attenuation of the LH surge. The maximum seasonal mean concentrations was used to represent a 3-month average exposure period, and the relevant intermediate-term and chronic effect (attenuation of the LH surge, considered a biomarker indicative of atrazine's ability to alter hypothalamic-pituitary function) is seen in the test animals after 1 month at doses of 40 mg/kg/day (lowest observed adverse effect level from Morseth 1996a) and after 4 to 5 months of daily exposure at 3.65 mg/kg/day (lowest observed adverse effect level from Morseth 1996b).

HED has a relatively high level of confidence in the estimates of risk for people using surface water-sourced CWS, because although conservative, they are refined in that they are based on monitoring data in finished drinking water from the PLEX, the VMS, and the ARP databases. This assessment for exposures to atrazine and the chlorinated metabolites in drinking water, is based on a solid foundation of available, reliable, and appropriate monitoring data relative to exposure assessments for most pesticides in drinking water. There is some uncertainty because the PLEX database, although large, is not comprehensive. There are individuals receiving drinking water from sources serving less than 25 people that are not regulated under the SDWA, and therefore, no monitoring data were available for the populations served by these CWS. Also, there are approximately 10,000 CWS receiving waivers from the requirement to monitor for atrazine based on sequential sampling showing low to non-detectable residues of atrazine in finished drinking water or by showing that atrazine use is not expected to impact the CWS. However, the risk estimates provided in this document assume that the waivers granted to those CWS were justified, and insignificant exposure to atrazine residues from those CWS are expected. Because PLEX includes those CWS detecting atrazine residues, the Environmental Fate and Effects Division (EFED) has reported the PLEX database to be conservatively biased. Both the VMS and the ARP programs are strongly conservatively biased. The VMS program includes only those CWS targeted as having the highest concentrations of atrazine based on the PLEX data, and are associated with contamination problems. The VMS was designed to partially offset the negative bias introduced into the PLEX database as a result of the infrequent sampling required under the SDWA. Although CWS selected for inclusion into the ARP program were chosen randomly, a stratified design was used to over select for CWS located in small watersheds with high atrazine use. Because of the way in which CWS were selected for inclusion into the VMS and ARP programs, and the more frequent sampling schedule used in

the VMS and ARP, the CWS in these two databases represent a high quality data set for estimating the high-end of exposures to atrazine residues expected in CWS using surface water.

There are some CWS using surface water with maximum measured concentrations of atrazine and the chlorinated metabolites approaching chronic DWLOC values for infants and children's groups, but whose annual average concentrations are below chronic DWLOC values that were not included in either of the more intensive sampling programs sponsored by industry. As a result, there are no seasonal mean concentrations for these CWS to compare to chronic DWLOC values. These CWS may have seasonal mean concentrations either above or below chronic DWLOC values. Although a direct comparison of these maximum measured concentrations to chronic DWLOC values would be inappropriate, this finding introduces another source of uncertainty into this risk assessment as it cannot be known from the available data if these CWS have seasonal mean concentrations of atrazine residues above levels of concern. Some of these CWS are listed in Appendix E for OW use in consideration of any necessary actions for these CWS.

For the portion of the U.S. population receiving their drinking water from rural private wells adjacent to atrazine use areas, there is high uncertainty associated with this risk estimate. The database represents potential high-end exposures of individuals to atrazine residues in private rural wells. This database is neither comprehensive nor were the wells included in this database chosen randomly. Wells sampled under the Novartis Rural Well Survey were targeted based on their proximity to atrazine use areas, well depth, and accessibility giving this database a very conservative bias. Risk estimates based on this database represent high-end exposures for individuals using rural wells. Because the wells were sampled only once, the possibility of missing higher one-day concentrations of atrazine residues in a well exists, in which case, the risk estimates given here may underestimate risk. However, HED notes that it is highly unlikely that under normal agricultural uses that atrazine residues would exceed a maximum one-day concentration of 298 ppb in a given well. The possibility of a long-term average being less than the single concentration value used gives the chronic exposure assessments a conservative bias.

For the portion of the U.S. population receiving their drinking water from CWS using groundwater as the source (73,856,519 people), HED notes that a partial, but incomplete estimate of risk indicates that exposures of this population to atrazine residues in finished drinking water are of less concern than exposures of the population receiving drinking water from surface water-sourced CWS. However, HED reserves its risk estimates for populations on CWS using groundwater until data are available to estimate the chlorinated metabolites. The lack of monitoring data on the chlorinated metabolites may underestimate exposure to atrazine residues of concern.

Hydroxy Metabolites

The main source of uncertainty regarding the hydroxy metabolites of atrazine is the lack of monitoring data. However, given the likely concentrations of these compounds in drinking water relative to their toxicity, HED does not expect exposure to these compounds to pose a significant risk.

4.3 OCCUPATIONAL EXPOSURE

HED has determined that there is the potential for short-term (1 to 30 days) and intermediate-term (30 days to several months) dermal and inhalation exposures of mixers, loaders, and applicators handling atrazine during application associated with the registered uses of atrazine. HED has also determined that there is the potential for short-term and intermediate-term post application dermal exposures to atrazine from harvesting activities. Long-term (chronic) occupational exposures of several months to lifetime duration are not anticipated.

For the purposes of incorporating short-term dermal exposures into occupational risk assessments, HIARC selected a dermal endpoint based on decreased body weight gains and food consumption from a 21-day dermal toxicity study in the rat. The NOAEL from this study was 100 mg/kg/day, and is multiplied by the rat/human relative penetration factor of 3.6 to obtain the NOAEL of 360 mg/kg/day relevant to human absorption of atrazine through the skin. For the purposes of incorporating short-term inhalation exposures into occupational risk assessments, HIARC selected an endpoint based on decreased body weight gain and food consumption from an oral developmental study in rats, which had a NOAEL of 10 mg/kg/day. An absorption factor of 100% is applied for inhalation exposures. Because the short-term dermal and inhalation endpoints chosen for risk assessment are based on the same toxic effects, dermal and inhalation exposures can be aggregated.

For the purposes of incorporating intermediate-term dermal exposure into occupational risk assessments, an oral endpoint was selected based on attenuation of the pre-ovulatory LH surge in a subchronic study in Sprague-Dawley rats with a NOAEL of 1.8 mg/kg/day. The committee recommended a dermal absorption factor of 6% based on a human study in which 10 human volunteers were exposed to a single topical dose of atrazine. The resulting endpoint for the purposes of incorporating intermediate-term dermal exposures into occupational risk assessments is 30 mg/kg/day. For the purposes of incorporating intermediate-term inhalation exposures into occupational risk assessments, the HIARC selected an endpoint from oral studies, because of a lack of inhalation studies. The same oral endpoint selected for intermediate-term dermal exposure (1.8 mg/kg/day) was selected for intermediate-term inhalation exposure. Because the dermal and inhalation endpoints for intermediate-term exposure are based on the same toxic effect, they may be aggregated.

The target margin of exposure (MOE) of 100 or more for occupational exposure scenarios was selected based upon 10x uncertainty factor (UF) for intraspecies and 10x UF for interspecies variation.

4.3.1 Handler

The Agency has determined that there are potential exposures to mixers, loaders, applicators, and other handlers during usual use-patterns associated with atrazine. Fifteen major exposure scenarios were identified for atrazine, including mixing, loading, and applying using aerial, ground spray, granular, fertilizer admixture, and lawn application methods. The major handler scenarios involved multiple crops and application rates, resulting in 139 different exposure estimates. The largest agricultural use of atrazine, and the largest potentially exposed occupational population, involves the mixing, loading and application of atrazine to row crops. Most of the occupational exposure studies submitted by the registrant have measured exposure of these workers. Several studies monitored potential dermal and inhalation exposure

to full time mixer/loaders and applicators in the corn belt. These studies used either passive dosimeters, urine biomonitoring, or both. All of the passive dosimetry studies reported residues in terms of the parent compound, atrazine, only. The biomonitoring studies measured urinary chlorotriazines and back-calculated atrazine dose.

The Agency also reviewed an agricultural handler study that included both passive dosimetry and biomonitoring of urinary metabolites of atrazine, and found the unit exposures were within one order of magnitude of the values in the Pesticide Handler Exposure Database (PHED) v. 1.1. The PHED is used by the Agency as a surrogate chemical database for handler exposure values. The passive dosimetry study was re-submitted by the registrant, in combination with the Agency's PHED values for ground applicators using enclosed systems. This was included as part of the risk estimates and compared to PHED-based estimates for agricultural handlers using closed systems, with reasonable agreement. Another study using biomonitoring to determine worker exposure included over 100 replicates, but did not meet adequate quality control criteria to allow the results to be related the quantity of atrazine handled. Instead, the range of daily dose per "typical" agricultural handler of atrazine in various formulations, using a variety of protective gear and application systems, confirms the findings of the other biomonitoring study and supports the overall agricultural handler risk assessment based on passive dosimetry.

The Outdoor Residential Exposure Task Force also submitted exposure studies to the Agency for either occupational or non-occupational residential applicator exposure. Those studies include application of granular formulations by push-spreader, profession lawn care operators using truck-mounted hoses with hand-gun controlled spray, resident-applicator using a granular push spreader, and resident-applicator using a hose-end spray.

The Agency estimated exposure to commercial handlers engaged in impregnating atrazine onto dry bulk fertilizer using dermal and inhalation unit exposure data from the PHED scenario for mixing/loading liquids using a closed system. However, such an exposure surrogate is less appropriate for transferring the treated dry bulk fertilizer from the auger truck to the application equipment. There ares no data or reasonable surrogate available for this operation.

Estimates of Handler Risk

The risk estimates presented consider exposures at baseline, i.e., a single-layer of clothing, shoes, socks, and bare hands; exposures with additional protective clothing (PPE) consisting of gloves and coveralls, and exposures with engineering controls where closed mixing/loading and application equipment are used. For the detailed calculations of exposure and risk estimates, see Attachment VI.

Short-Term Exposures (1 to 30 days):

For short-term exposure estimates based on either PHED data, chemical specific exposure studies, and/or ORETF data, with appropriate personal protective equipment (PPE) or engineering controls, all short-term aggregate (dermal and inhalation) handler exposure scenarios had MOEs greater than 100, and thus, do not exceed HED's level of concern. There were no exposure data for liquid/liquid fertilizer treatment, so risk estimates for this scenario could not be calculated.

Based solely on PHED data, and after consideration of personal protective equipment (PPE) or engineering controls, all short-term aggregate (dermal and inhalation) exposure scenarios had MOEs

greater than 100. Engineering control methods were only required to mitigate exposure for one scenario.

The chemical specific passive dosimetry and biomonitoring studies support the PHED assessment. In these studies, the handlers monitored for the most part used closed mixing and loading systems and enclosed cab sprayers (that is, they incorporate PPE and engineering controls). From the combined passive dosimetry/biomontoring handler study, the 90th percentile biomonitoring values provided short-term estimated MOEs of 100-400 for mixing, loading, and applying liquid formulation by groundboom. The passive dosimetry 90th percentile exposure data for the same handler scenarios produced MOEs ranging from 130 to 390. Using the 90th percentile of the biomonitoring-only study data, normalized to body weight, short-term daily MOEs greater than 100 (range 740-2600) were estimated for all mixers, loaders, applicators, and mixer/loader/applicators applying ground spray to corn.

Using the ORETF study data, where applicable, baseline short-term MOEs for lawn care operators (LCOs) spraying lawns or applying granular formulations were all greater than 100. Where PHED data were used, all LCO scenarios had MOEs greater than 100 with the use of gloves. Table 15 shows the estimated short-term exposures and risks for handlers for the specific scenarios assessed. Table 16 shows the short-term risk estimates for LCOs handling atrazine. The reader is referred to Attachment VI for details.

Intermediate-term Exposures (30 days to several months):

For intermediate-term exposure estimates based on either PHED data, chemical specific exposure studies, or a combination of these data, with appropriate personal protective equipment (PPE) or engineering controls, most (approximately 80%) intermediate-term aggregate (dermal and inhalation) handler exposure scenarios had MOEs greater than 100, and thus, do not exceed HED's level of concern. There were no exposure data for liquid/liquid fertilizer treatment, so risk estimates for this scenario could not be calculated.

Using PHED data incorporating PPE and/or engineering controls, 109 of the 139 (78%) of the handler exposure scenarios had intermediate-term aggregate (dermal and inhalation) MOEs greater than 100. There were no data for liquid/liquid fertilizer treatment and the right-of-way and hand sprays had no known engineering controls.
Using the corn applicator study/PHED combined data, with engineering controls, 51 of 62 applicable handler scenarios (82%) had MOEs greater than100. Using the passive dosimetry study data alone, which reflected the use of engineering controls, the geometric means of the estimated doses result in handler MOEs of 210-520. Biomonitoring study data for handlers using mostly engineering controls provided estimated MOES of 69-1600 using the geometric mean for each task. Some MOEs were less than 100 when based on the 90th percentile study doses. Using the ORETF study data, all baseline clothing intermediate-term lawn care operator (LCO) handler scenarios had MOEs greater than 100. Where PHED data was used, LCO handlers required additional PPE to achieve MOEs greater than 100.

Intermediate-term exposures that exceed HED's level of concern are generally associated with mixing and loading of the largest quantities (liquid or dry flowable/WDG) of atrazine. Examples include the higher application rates and acerages for use on chemical fallow lands, grasslands, corn, sorghum, and in fertilizer

admixture. With engineering controls, all applicator risk estimates have MOEs above 100. Table 15 shows the estimated intermediate-term exposures and risks for handlers for the specific scenarios assessed. Table 16 shows the intermediate-term risk estimates for LCOs handling atrazine. The reader is referred to Attachment VI for details.

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Mixer/Loader									
Mixing/Loading Liquid Formulations for Aerial Application (1a)	Conifer forests, sugarcane, conifer (Christmas tree) farms, sod farms in FL	4	350	6	0.44	**540**	61	1,500	**130**
	sugarcane	2.6	350	9	0.68	**840**	94	2,300	**200**
	chemical fallow	3	1,200	2	0.17	**210**	24	580	50
			350	8	0.59	**730**	82	2,000	**170**
		1.4	1,200	5	0.37	**450**	51 g,dl	1,200	**110**
			350	17	1.3	**1600**	**99 g,dl**	4,300	370 (NN)
	CRP or grasslands	2	1,200	4	0.26	**320**	36	870	75
			350	12	0.88	**1100**	**120**	3,000	260 (NN)
	corn, sorghum	2	1,200	4	0.26	**320**	36	870	**75**
			350	12	0.88	**1100**	**120**	3,000	260 (NN)
		1	1,200	7	0.51	**630**	71	1,700	**150**
			350	24	1.8	**2200**	**120 g**	6,000	520 (NN)
	sod farms	2	350	12	0.88	**1100**	**120**	3,000	260 (NN)

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Mixing/Loading Liquid Formulations for Groundboom Application (1b)	sugar cane, macadamia nuts, guava, conifers, sod farms in FL	4	80	27	1.9	**2400**	**130 g**	6,500	560 (NN)
	sugarcane	2.6	80	41	3.0	**3700**	**200 g**	10,000	870 (NN)
	chemical fallow	3	450	6	0.46	**560**	63	1,500	**130**
			200	14	1.0	**1300**	**110 g,r**	3,500	300 (NN)
		1.4	450	14	0.98	**1200**	**110 g,r**	3,300	290 (NN)
			200	31	2.2	**2700**	**150 g**	7,500	640 (NN)
	CRP/grasslands	2	450	9	0.68	**850**	95	2,300	**200**
			200	21	1.5	**1900**	**100 g**	5,200	450 (NN)
	corn, sorghum	2	450	9	0.68	**850**	95	2,300	**200**
			200	21	1.5	**1900**	**100 g**	5,200	450 (NN)
		1	450	19	1.4	**1700**	**110 g,dl**	4,600	400 (NN)
			200	43	3.1	**3800**	**210 g**	10,000	900 (NN)
	roadsides	1	40	210	15	19000	**1,000 g**	52,000	4,500 (NN)
	Bermuda grass rights-of-way	4	40	53	3.9	**4800**	**260 g**	13,000	1,100 (NN)
	golf course turf	2	40	110	7.7	9500	**520 g**	26,000	2,300 (NN)
	sod farms	2	80	53	3.9	**4800**	**260 g**	13,000	1,100 (NN)
Mixing/Loading Liquid Formulations for Rights-of-Way Sprayer (1c)	roadsides	1	40	210	15	19000	**1,000 g**	52,000	4,500 (NN)
	Bermuda grass hwy rights-of-way	4	40	53	3.9	**4800**	**260 g**	13,000	1,100 (NN)

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Mixing/Loading Liquid Formulations for Lawn Handgun Application (LCO) (1d)	lawns, golf courses	2	100	43	3.1	**3800**	**210 g**	10,000	900 (NN)
Mixing/Loading/ Incorporating Liquid Formulations onto Dry Bulk Fertilizer (1e)	commercial fertilizer for corn, sorghum	2	NA 700 lb fert/day	See Engineering Controls				110	9
			NA 400 lb fert/day	See Engineering Controls				220	19
			NA 200 lb fert/day	See Engineering Controls				380	33
	commercial fertilizer for corn, sorghum	1	NA 700 lb fert/day	See Engineering Controls				220	19
			NA 400 lb fert/day	See Engineering Controls				430	38
			NA 200 lb fert/day	See Engineering Controls				760	66
	on-farm fertilizer for corn, sorghum	2	500	8.5	0.62	**760**	86	2,100	**180**
			250	17	1.2	**1500**	**97 g,dl**	4,100	360 (NN)
			143	30	2.2	**2700**	**150 g**	7,300	630 (NN)
		1	500	17	1.2	**1500**	**97 g,dl**	4,100	360 (NN)
			250	34	2.4	**3000**	**170 g**	8,300	720 (NN)
			143	60	4.3	**5300**	**290 g**	15,000	1,300 (NN)

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Mixing/Loading Liquid Formulations into Liquid Bulk Fertilizer at Commercial Operations (1f)	fertilizer for corn, sorghum	2	UNK	No Data					
			UNK	No Data					
			UNK	No Data					
		1	UNK	No Data					
			UNK	No Data					
			UNK	No Data					
Mixing/Loading Dry Flowable (Water Dispersible Granule) for Aerial (2a)	conifer forests, sugarcane, conifer (Christmas tree) farms, turf for sod in FL	4	350	180	16	250	26	910	93
	sugarcane	2.6	350	280	25	380	40	1,400	**140**
	chemical fallow	3	1,200	71	6.3	97	10	350	36
			350	240	22	330	35	1,200	**120**
		1.4	1,200	150	14	210	22	760	78
			350	520	47	710	61 g,dl	2,600	**270**
	CRP or grasslands	2	1,200	110	9.5	140	15	520	54
			350	370	33	500	43 g,dl	1,800	**190**
	corn, sorghum	2	1,200	110	9.5	140	15	520	54
			350	370	33	500	43 g,dl	1,800	**190**
		1	1,200	210	19	290	30	1,100	**110**
			350	730	65	990	86 g,dl	3,600	**370**
	sod farms	2	350	370	33	500	43 g,dl	1,800	**190**

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Mixing/Loading Dry Flowables (water dispersible) for Groundboom Application (2b)	sugar cane, macadamia nuts, guava, conifers, sod farms in FL	4	80	800	71	1100 (NN)	94 g,dl	4,000	**410**
	sugarcane	2.6	80	1200	**110**	1700	110 g (NN)	6,100	630 (NN)
	chemical fallow	3	450	190	17	260	27	950	97
			200	430	38	580	50 g,dl	2,100	**220**
		1.4	450	410	36	550	48 g,dl	2000	**210**
			200	920	82	1200	**110 g,dl**	4500	470 (NN)
	CRP or grasslands	2	450	280	25	390	40	1400	**140**
			200	640	57	870	75 g,dl	3200	**330**
	corn, sorghum	2	450	280	25	390	40	1400	**140**
			200	640	57	870	75 g,dl	3200	**330**
		1	450	570	51	770	67 g,dl	2800	**290**
			200	1300	**110**	1700	150 g,dl (NN)	6500	650 (NN)
	roadsides	1	40	6400	**570**	8700	570 g (NN)	32,000	3,300 (NN)
	Bermuda grass rights- of- way	4	40	1600	**140**	2200	140 g (NN)	8000	820 (NN)
	golf course turf	2	40	3200	**290**	4300	290 g (NN)	16,000	1,600 (NN)
	sod farms	2	80	1600	**140**	2200	140 g (NN)	8000	820 (NN)
Mixing/Loading Dry Flowables (water dispersible) for Rights of Way (2c)	roadsides	1	40	6400	**570**	8700	570 g (NN)	32,000	3,300 (NN)
	Bermuda grass hwy rights-of-way	4	40	1600	**140**	2200	140 g (NN)	8000	820 (NN)
Loading Granular Formulations (3)	sod farms	2	80	2000	**310**	7400	320 g (NN)	98,000	15,000 (NN)
	golf course turf	2	40	3900	**610**	15000	640 g (NN)	200,000	31,000 (NN)
Applicator									

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Applying Liquids with Aircraft (4)	conifer forests, sugarcane, conifer (Christmas tree) farms, sod farms in FL	4	350	See Engineering Controls				2,300	**210**
	sugarcane	2.6	350	See Engineering Controls				3,500	**320**
	chemical fallow	3	1,200	See Engineering Controls				900	82
			350	See Engineering Controls				3,100	**280**
		1.4	1,200	See Engineering Controls				1,900	**170**
			350	See Engineering Controls				6,500	**600**
	CRP or grasslands	2	1,200	See Engineering Controls				1,300	**120**
			350	See Engineering Controls				4,600	**420**
	corn, sorghum	2	1,200	See Engineering Controls				1,300	**120**
			350	See Engineering Controls				4,600	**420**
		1	1,200	See Engineering Controls				2,700	**240**
			350	See Engineering Controls				9,100	**840**
	sod farms	2	350	See Engineering Controls				4,600	

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Applying Liquids for Groundboom Application (5)	sugar cane, macadamia nuts, guava, conifers, sod farms in FL	4	80	1700	**210**	3900 (NN)	210 g (NN)	12,000	980 (NN)
	sugarcane	2.6	80	2700	**330**	6000	330 g (NN)	18,000	1,500 (NN)
	chemical fallow	3	450	410	51	920	**99**	2,700	**230**
			200	930	**110**	2100	110 g (NN)	6,200	520 (NN)
		1.4	450	890	**110**	2000	110 g (NN)	5,900	500 (NN)
			200	2000	**240**	4500	240 g (NN)	13,000	1,100 (NN)
	CRP or grasslands	2	450	620	76	1400	**120 g,r**	4,100	350 (NN)
			200	1400	**170**	3100	170 g (NN)	9,300	790 (NN)
	corn, sorghum	2	450	620	76	1400	**120 g,r**	4,100	350 (NN)
			200	1400	**170**	3100	170 g (NN)	9,300	790 (NN)
		1	450	1200	**150**	2800	150 g (NN)	8,200	700 (NN)
			200	2800	**340**	6200	340 g (NN)	19,000	1,600 (NN)
	Bermuda grass hwy rights-of-way	4	40	3500	**430**	7800	430 g (NN)	23,000	2,000 (NN)
	roadsides	1	40	14000	**1,700**	31000	1,700 g (NN)	93,000	7,900 (NN)
	golf course turf	2	40	7000	**850**	16000	850 g (NN)	46,000	3,900 (NN)
	sod farms	2	80	3500	**430**	7800	430 g (NN)	23,000	2,000 (NN)
Applying Liquids with a Rights-of-Way Sprayer (6)	Bermuda grass rights-of-way	4	40	110	8.2	370	37	NF	NF
	roadsides	1		430	33	1500	**99 g**	NF (NN)	NF (NN)
Applying Liquids with a Handgun (7)	lawns, golf courses	2	5	NA	see PPE	7200	**500 g**	NF (NN)	NF (NN)

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Applying Impregnated Dry Bulk Granular Fertilizer with Tractor Drawn Spreader(8)	corn, sorghum	2	500	420	60	1500 (NN)	**160 g,r**	2,200	320 (NN)
			250	840	**120**	2900	130 g (NN)	4,500	640 (NN)
			143	1500	**210**	5100	230 g (NN)	7,800	1,100 (NN)
		1	500	840	**120**	2900	130 g (NN)	4,500	640 (NN)
			250	1700	**240**	5800	260 g (NN)	9,000	1,300 (NN)
			143	2900	**420**	10000	460 g (NN)	16,000	2,200 (NN)
Applying Granular with a Tractor Drawn Spreader (9)	on farm fertilizer for corn, sorghum	2	200	1000	**150**	3600	170 g (NN)	5,600	790 (NN)
			80	2600	**380**	9100	410 g (NN)	14,000	2,000 (NN)
		1	200	2100	**300**	7300	330 g (NN)	11,000	1,600 (NN)
			80	5200	**750**	18000	830 g (NN)	28,000	4,000 (NN)
	golf course turf	2	40	5200	**750**	18000	830 g (NN)	28,000	4,000 (NN)
Mixer/Loader/Applicator									
Backpack Sprayer: Liquid Formulations (LCO) (10)	lawns, golf courses	2	1	NA	none, see PPE	**4500**	350g,	NF (NN)	NF (NN)
Low Pressure Handwand - Liquid Formulations (LCO) (11)	lawns, golf courses	2	1	**130**	9	18,000	1700 g	NF (NN)	NF (NN)
Lawn Handgun (and Compressed Air Sprayer) (liquid formulations) (LCO) (12)	lawns, golf courses	2	5	NA	none, see PPE	**6600**	**450 g**	12,000 (eng = M/L only)	870 (NN) (eng = M/L only)
Granulars with a Push Type Spreader (LCO) (13)	lawns, golf courses	2	5	4400	60	1900 (NN)	**130 g**	NF (NN)	NF (NN)

Table 15: Summary of Occupational Short-term and Intermediate-term Handler Risks from Atrazine (Using PHED Data)									
Handler Scenario				Baseline MOEs[c]		PPE MOEs[c]		Engineering Control MOEs[e]	
				Short-term	Intermediate-term	Short-term	Intermediate-term	Short-term	Intermediate-term
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre or lb ai/gal)	Area Treated Per Day[b] (Acres)	Aggregate Dermal + Inhalation	Aggregate Dermal + Inhalation	Aggregate: with gloves unless noted and with dust/mist respirator	Aggregate with gloves + double layers + respirator, unless noted	Aggregate Dermal + Inhalation (NN at all scenarios)	Aggregate Dermal + Inhalation
Granulars with a Bellygrinder (LCO) (14)	lawns, golf courses	2	1	1000	82	1300 (NN)	**95 g,r 130 g,dl**	NF	NF
Flagging									
Flagging Sprays (15)	conifer forest, sugarcane, conifer (Christmas tree) farms, sod farms	4	350	700	76	1400 dl (NN)	81 dl	2,600	**220**
	sugarcane	2.6	350	1100	**120**	2100 dl (NN)	120 dl (NN)	4,000	350 (NN)
	chemical fallow	3	350	930	**100**	1900 dl (NN)	110 dl	3,500	300 (NN)
		1.4	350	2000	**220**	4000 dl (NN)	230 dl (NN)	7,500	640 (NN)
	CRP or grasslands	2	1,200	410	45	810 dl (NN)	67 dl,r	1,500	**130**
			350	1400	**150**	2800 dl (NN)	160 dl (NN)	5,300	450 (NN)
	corn, sorghum	2	1,200	410	45	810 dl (NN)	67 dl,r	1,500	**130**
			350	1400	**150**	2800 dl (NN)	160 dl (NN)	5,300	450 (NN)
		1	1,200	820	89	1600 dl (NN)	95 dl	3,100	**260**
			350	2800	**310**	5600 dl (NN)	320 dl (NN)	11,000	900 (NN)
	sod farms	2	350	1400	**150**	2800 dl (NN)	160 dl (NN)	5,300	450 (NN)

Footnotes:

a Application rates represent maximum rates determined from EPA registered labels for atrazine. Typical use rates as determined by BEAD were assessed for corn and sorghum (1.0 lb ai/acre), sugarcane (2.6 lb ai/acre) and chemical fallow (1.4 lb ai/acre).

b Area Treated (acres treated per day) based on Exposure SAC Policy # 9 "Standard Values for Daily Acres Treated In Agriculture," Revised June 23, 2000.

c Baseline MOEs: see Occupational Short-term and Intermediate-term Handler Risks from Atrazine at Baseline Table.

d PPE MOEs: see Occupational Short-term and Intermediate-term Handler Risks from Atrazine with PPE Risk Mitigation Table.

e Engineering Control MOEs: see Occupational Short-term and Intermediate-term Handler Risks from Atrazine with Engineering Controls Table.

UNK = Unknown -- additional use information needed
NN = Not needed -- MOE > 100 at previous risk mitigation level

NF = Not feasible -- no engineering control known for this application method
Bold = uncertainty factor (MOE) reached or exceeded at that risk mitigation level
Shaded = uncertainty factor (MOE) not attained at maximum feasible risk mitigation
dl = double layer clothing (coveralls over single layer)
g = gloves
r = respirator

Table 16: Occupational Handler Short-Term and Intermediate-Term Risks for LCO's Applying Atrazine (assessed using ORETF unit exposure values)

Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre)	Acres Treated Per Day[b]	Baseline Unit Exposure Values		Baseline Short-Term Risks				Baseline Intermediate-Term Risks				
						Daily Dose (mg/kg/day)		MOEs		Daily Dose[e] (mg/kg/day)		MOEs		
				Dermal[c] (mg/lb ai)	Inhalation[d] (µg/lb ai)	Dermal[e]	Inhalation[f]	Dermal[g]	Inhalation[h]	Dermal[e]	Inhalation[f]	Dermal[g]	Inhalation[h]	Aggregate[i]
Mixer/Loader/Applicator														
Lawn Handgun (and Compressed Air Sprayer) (liquid formulations) (12a)	lawns, golf courses	2	5	0.69	1.5	0.099	0.00025	3,700	40,000	0.0069	0.00025	260	7,200	250
Lawn Handgun (and Compressed Air Sprayer) - (water dispersible granules) (12b)				0.92	22	0.13	0.0037	2,700	2,700	0.0092	0.0037	200	490	140
Lawn Handgun (and Compressed Air Sprayer) - (water soluble bag packaging) (12c)				0.96	7.7	0.14	0.0013	2,600	7,800	0.0096	0.0013	190	1,400	170
Granulars with a Push Type Spreader (13)				0.31	14	0.044	0.0023	8,100	4,300	0.0031	0.0023	580	770	330

Footnotes:

a Application rates represent maximum rates determined from EPA registered labels for atrazine.
b Acres treated per day values are EPA estimates found in Exposure SAC Policy # 9 "*Standard Values for Daily Acres Treated in Agriculture*", revised June 23, 2000.
c Dermal unit exposure values (geometric mean values) from 2 Outdoor Residential Exposure Task Force studies (ORETF Study Number OMA001 and OMA002). Unit exposure data were analyzed in 2 EPA draft memos, dated October 19, 2000 " *Exposure of Professional Lawn Care Workers During the Mixing, Loading, and Application of Granular Turf Pesticides Utilizing a Surrogate Compound* and "Exposure of Professional Lawn Care Workers During the Mixing and Loading of Dry and Liquid Application of Turf Pesticides Utilizing a Surrogate Compound. LCO exposure was assessed in this table assuming a long pants, long sleeved shirt , no gloves clothing scenario.
d Inhalation unit exposure values from the same ORETF studies cited in footnote c and assuming a no respirator scenario.
e Dermal daily dose (mg/kg/day) = daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x area treated per day (acres/day) / body weight (70 kg adult for short-term and 60 kg developmental female for intermediate-term). A 6% dermal absorption factor applies for intermediate-term dermal dose.
f Inhalation daily dose (mg/kg/day) = inhalation unit exposure (µg/lb ai) x application rate (lb ai/acre) x area treated per day (acres/day) x conversion factor (1 mg/1,000 µg) / body weight (60 kg female for both short- and intermediate-term).
g Dermal MOE = NOAEL (360 mg/kg/day for short-term and 1.8 mg/kg/day for intermediate-term) / daily dermal dose (mg/kg/day).
h Inhalation MOE = NOAEL (10 mg/kg/day for short-term and 1.8 mg/kg/day for intermediate-term) / daily inhalation dose (mg/kg/day).
i Aggregate MOE for intermediate-term assessments = NOAEL (1.8 mg/kg/day) / absorbed daily dermal + inhalation dose (mg/kg/day)

4.3.2 Post Application

Estimates of Post Application Risk

Short-term and Intermediate-term Exposures:

Most of the atrazine used in agriculture is applied to corn and sorghum early in the season, either before weeds emerge (pre-emergence) or when the crops are quite small (generally less than 12 inches high). This fact, and the degree of mechanization in cultivating these crops, minimizes the Post application contact of workers with the chemical on these crops.

Three chemical-specific studies, one of dislodgeable foliar residue on corn, and two of transferable turf residues (TTR), were submitted to the Agency for consideration. All three were reviewed and found to acceptable for use in the atrazine risk assessment. Wherever possible, transfer coefficients (Tc) used in exposure calculations were based upon data submitted by the Agricultural Reentry Task Force (ARTF).

Using the average daily foliar residues from each study at day 0-1 and day 7 after treatment, all post application short- and intermediate-term dermal risk estimates were below the HED's level of concern (range 100 to 220,000). The lowest MOEs, for trimming/harvesting Christmas trees (120) and harvesting sod (100), used a combination of atrazine-specific study data (residue data for days 0 to1) and standard assumptions for worker activities to produce a high-end or screening-level exposure estimate. These latter assessments should also be adequate for use as surrogates for other exposure scenarios for which more data are needed, such as working with other tree crops and in sugarcane fields. Post application risk estimates given as MOEs are provided in Tables 17, 18, and 19 for harvesting activities, granular formulations applied to turf and nut crops, and liquid formulations applied to turf and nut crops, respectively. The reader is referred to Attachment VI for details.

Table 17. Occupational Short- and Intermediate-Term Postapplication Risks for Atrazine
(Using DFR values from Atrazine corn study MRID No. 448836-01)

Crop/Use Pattern	Application Rate (lb ai/acre)	Postapplication Activity	Transfer Coefficient[a]	Short Term Risks		Intermediate Term Risks	
				DFR[b] (µg/cm^2) (DAT 0-1)	MOE[c]	DFR[d] (ug/cm^2) (DAT 7)	MOE[e]
Corn	2	Scout (minimum foliage)	400	3.368	2,300	0.1024	5,500
		Irrigate, weed (minimum foliage)	100	3.368	9,400	0.1024	22,000
Conifer Forests	4	Scout	1,000	6.736	470	0.2048	1,100
Christmas Tree Farms	4	Stake, top, train, harvest (full foliage)	8,000	6.736 (DAT 0-1)	58 (DAT 0-1)	0.2048	140
				3.260 (DAT 1)	120 (DAT 1)		
		Prune	3,000	6.736	160	0.2048	370
		Scout, thin	1,000	6.736	470	0.2048	1,100
Sugarcane	4	Scout (full foliage)	2,000	6.736	230	0.2048	550
Sorghum	2	Scout, irrigate (minimum foliage)	100	3.368	9,400	0.1024	22,000

a Transfer coefficient from Science Advisory Council for Exposure: Policy Memo # 003 .1 "Agricultural Transfer Coefficients," Revised - August 7, 2000.

b DFR source: corn study MRID # 448836-01, DAT 0-1 residue unless an MOE of >100 was not reached. In such cases risks were assessed on days following application until an MOE of 100 was determined. The highest residue value occurring between DAT 0-1 was used for determination of DAT 1 MOE's. The highest residue values were detected after application of a 90 DF wettable powder formulation. The study was conducted using an application rate of 2.5 lb ai/acre. The residues were first normalized to reflect an application rate of 2.0 lb ai/acre to aid in determination of highest residues (i.e., the 90 DF vs 4L formulations). When assessing activities involving a different application rate than was used in the study, the DFR values were adjusted proportionately to reflect the different application rates. For example, for sugarcane, which has a maximum label rate of 4.0 lb ai/acre, adjusted DFR = $\frac{\text{Corn DFR} \times 4 \text{ lb ai/A for sugarcane}}{2 \text{ lb ai/A for corn}}$

c MOE = Short-term NOAEL (360 mg/kg/day; based on a dermal study) / dermal dose where dose = DFR (µg/cm^2) x TC (cm^2/hr) x conversion factor (1 mg/1,000 µg) x exposure time (8 hrs/day) / body weight (70 kg adult).

d DFR source: corn study MRID # 448836-01, DAT 7 residue. See footnote b for further explanation.

e MOE = Intermediate-term NOAEL (1.8 mg/kg/day; based on an oral developmental study) / absorbed dermal dose where absorbed dose = DFR (µg/cm^2) x TC (cm^2/hr) x conversion factor (1 mg/1,000 µg) x exposure time (8 hrs/day) x dermal absorption (6%) / body weight (60 kg developmental female).

Note: DFR = Dislodgeable Foliar Residue

Table 18: Occupational Short- and Intermediate-Term Postapplication Risks for Granular Atrazine Formulations
(Using TTR values from granular Atrazine turf study MRID No. 449588-01)

Crop/Use Pattern	Application Rate (lb ai/acre)	Postapplication Activity	Transfer Coefficient	Short Term Risks				Intermediate Term Risks			
				TTR[b] (ug/cm²) (DAT 0-1)		MOE[c]		TTR[d] (ug/cm²) (DAT 7)		MOE[e]	
				GA	FL	GA	FL	GA	FL	GA	FL
Golf Course Turf	2	Mow, seed, scout, mechanical weed, aerate, fertilize, prune	500	0.0585	0.216	110,000	29,000	0.0105	0.0393	43,000	11,000
		Transplant, high contact	16,500	0.0585	0.216	3,300	880	0.0105	0.0393	1,300	350
Sod Farms (FL)	4	Mow, scout, mechanical weed, irrigate	500	NA				0.021	0.0786	21,000	5,700
		Transplant, hand weed, harvest (hand or mechanical)	16,500	NA				0.021	0.0786	650	170
Sod Farms	2	Mow, scout, mechanical weed, irrigate	500	NA				0.0105	0.0393	43,000	11,000
		Transplant, hand weed, harvest (hand or mechanical)	16,500	NA				0.0105	0.0393	1,300	350
Macadamia Nuts/Guava	4	Mow, scout, irrigate (turf under the trees)	500	0.117	0.432	54,000	15,000	0.021	0.0786	21,000	5,700

a Transfer coefficient from Science Advisory Council for Exposure: Policy Memo # 003 .1 "Agricultural Transfer Coefficients," Revised - August 7, 2000.

b TTR source: granular atrazine to turf study MRID # 449588-01, DAT 0-1 residue. The highest residue value occurring between DAT 0-1 was used for determination of DAT 1 MOE's. The study was conducted in GA and FL using an application rate of 2.0 lb ai/acre. When assessing activities involving a different application rate than was used in the study, the TTR values were adjusted proportionately to reflect the different application rates. For example, for Bermuda grass rights of way, which have a maximum label rate of 4.0 lb ai/acre, adjusted

$$\text{TTR} = \frac{\text{Turf TTR x 4 lb ai/A for Bermuda grass rights of way}}{\text{2 lb ai/A for turf}}$$

c MOE = Short-term NOAEL (360 mg/kg/day; based on a dermal study) / dermal dose where absorbed dose = TTR (µg/cm²) x TC (cm²/hr) x conversion factor (1 mg/1,000 µg) x exposure time (8hrs/day)/ body weight (70 kg; adult).

d TTR source: granular atrazine turf study MRID # 449580-01, DAT 7 residue. See footnote b for further explanation.

e MOE = Intermediate-term NOAEL (1.8 mg/kg/day; based on an oral developmental study) / absorbed dermal dose where absorbed dose = TTR (µg/cm²) x TC (cm²/hr) x conversion factor (1 mg/1,000 µg) x exposure time (8 hrs/day) x dermal absorption (6 %) / body weight (60 kg; developmental female).

NA = Not applicable to this scenario.

TTR - Turf Transferable Residue

Table 19. Occupational Short- and Intermediate-Term Postapplication Risks for Liquid Atrazine Formulations
(Using TTR values from liquid Atrazine turf study MRID No. 449580-01)

Crop/Use Pattern	Application Rate (lb ai/acre)	Postapplication Activity	Transfer Coefficient[a] (TC)	Short Term Risks				Intermediate Term Risks			
				TTR[b] (ug/cm²) (DAT 0-1)		MOE[c]		TTR[d] (ug/cm²) (DAT 7)		MOE[e]	
				GA	NC	GA	NC	GA	NC	GA	NC
Golf Course Turf	2	Mow, seed, scout, mechanical weed, aerate, fertilize	500	0.241	1.32	26,000	4,800	0.0658	0.052	6,800	8,600
		Transplant, high contact	16,500	0.241	1.32	790	140	0.0658	0.052	210	260
Sod Farms (FL)	4	Mow, scout, mechanical weed, irrigate	500	NA				0.1316	0.1046	3,400	4,300
		Transplant, hand weed, harvest (hand or mechanical)	16,500	NA				0.1316	0.1046	100	130
Sod Farms	2	Mow, scout, mechanical weed, irrigate	500	NA				0.0658	0.052	6,800	8,600
		Transplant, harvest (hand or mechanical)	16,500	NA				0.0658	0.052	210	260
Macadamia Nuts/Guava	4	Mow, scout, irrigate (turf under the trees)	500	0.482	2.64	13,000	2,400	0.1316	0.1046	3,400	4,300

a Transfer coefficient from Science Advisory Council for Exposure: Policy Memo # 003 .1 "Agricultural Transfer Coefficients," Revised - August 7, 2000.

b TTR source: liquid atrazine to turf study MRID # 449580-01, DAT 0-1 residue unless an MOE of >100 was not reached. In such cases risks were assessed on days following application until an MOE of 100 was determined. The highest residue value occurring between DAT 0-1 was used for determination of DAT 1 MOE's. The study was conducted in GA and NC using an application rate of 2.0 lb ai/acre. When assessing activities involving a different application rate than was used in the study, the TTR values were adjusted proportionately to reflect the different application rates. For example, for Bermuda grass rights of way, which have a maximum label rate of 4.0 lb ai/acre, adjusted TTR =

$$\frac{\text{Turf TTR} \times \text{4 lb ai/A for Bermuda grass rights of way}}{\text{2 lb ai/A for turf}}$$

c MOE = Short-term NOAEL (360 mg/kg/day; based on a dermal study) / dermal dose where dose = TTR (µg/cm²) x TC (cm²/hr) x conversion factor (1 mg/1,000 µg) x exposure time (8 hrs/day) / body weight (70 kg adult).

d TTR source: liquid atrazine turf study MRID # 449580-01, DAT 7 residue. See footnote b for further explanation.

e MOE = Intermediate-term NOAEL (1.8 mg/kg/day; based on an oral developmental study) / absorbed dermal dose where absorbed dose = TTR (µg/cm²) x TC (cm²/hr) x conversion factor (1 mg/1,000 µg) x exposure time (8 hrs/day) x dermal absorption (6%) / body weight (60 kg female).

NA = Not applicable to this scenario.

TTR = Turf Transferable Residue

Incident reports

Based on occupational incident data, atrazine appears to have fewer reported cases with moderate or major effects than other major pesticides. Non-occupational cases showed a greater frequency of cases with moderate and major effects as well as cases requiring treatment than occupational cases. However, this was based on a relatively small number of cases and there was evidence that these effects may have been coincidental with rather than because of exposure.

For incidents involving children under six years of age, atrazine exposure was most likely to result in minor or moderate symptoms. But it should be noted this was based on relatively few cases: seven children with minor symptoms and two children with moderate symptoms. Dermal and ocular effects accounted for the majority of symptoms associated with exposure to atrazine, though a number of cases also reported gastrointestinal, neurological, and respiratory effects.

California data collected from 1982 through 1996 detailed one case submitted to the California Pesticide Illness Surveillance Program (1982-1996). In this case, a worker used the product to contribute to the production of a commodity. Specific symptoms were not mentioned. On the list of the top 200 chemicals for which the National Pesticide Telephone Network received calls from 1984-1991 inclusively, atrazine was ranked 33rd with 117 incidents in humans reported and 28 incidents in animals (mostly pets). From the review of the Incident Data System, it appears that a majority of cases involved skin illnesses such as dermal irritation and pain, rashes, and welts and eye illnesses such as eye damage, blurred vision, conjunctivitis, irritation, and pain. Poison Control Center data tend to support these findings. Dermal and ocular effects were the most common effects reported due to occupational exposure.

HED concludes that none of the epidemiologic studies reviewed add significant new information concerning the adverse health effects of atrazine. A non-significant elevation in non-Hodgkin's lymphoma (NHL) continues to be observed at the Louisiana plant among workers exposed to triazines, including atrazine. By itself, this study does not support a conclusion of increased cancer from exposure to triazines. However, this study could be considered supportive, but only supportive and not definitive, if evidence of an association between non-Hodgkin's lymphoma and triazine exposure was available from other studies. Follow-up by the National Cancer Institute in four states looked specifically to determine whether earlier associations in individuals studies could be attributed to atrazine when adjustment was made for exposures to other pesticides. They concluded that "detailed analyses suggested that there was little or no increase in the risk of NHL attributable to the agricultural use of atrazine" (Zahm et al. 1993). In January, 2000, Dr. Ruth H. Allen of the Agency reviewed five epidemiological studies with findings related to atrazine, including cancer incidence. The most statistically significant findings related ovarian cancer and atrazine exposure among workers in a corn growing region of Italy. However, there are no studies from other regions to confirm these findings. Other types of cancer in the U.S. were not found to have statistically significant correlation to atrazine exposure.

No major literature citations were found concerning poisoning incidents due to atrazine. There are a number of cancer epidemiology studies of atrazine or triazine herbicides as a group, several of which have been previously reviewed by HED.

4.4 RESIDENTIAL EXPOSURE

Atrazine is labeled for homeowner use to control weeds in turf grass. Homeowners applying atrazine products to their lawns may be exposed to atrazine through their skin (dermal) and by inhaling dusts or sprays (inhalation) during application. Residential exposures to atrazine are expected to be short-term in duration from 1 day to a maximum of 2 to 3 weeks. Intermediate-term exposures greater than 30 days in duration are not anticipated from residential uses of atrazine. The following five residential handler exposure scenarios were evaluated:

(1) mixing, loading, and applying liquid formulations using a backpack sprayer,
(2) mixing, loading, and applying liquid and wettable powder formulations with a low pressure hand wand,
(3) mixing, loading, and applying liquid (ready-to-use) formulations with a hose-end sprayer,
(4) mixing, loading, and applying granulated formulations with a push-type spreader,
(5) mixing, loading, and applying granulated formulations with a belly grinder.

Toddlers (1 to 3 years old) have the potential to be exposed to atrazine residues after application through a transfer of residues to the skin (dermally) and through incidental oral exposure routes, such as, hand-to mouth, and soil and turf ingestion. Adults may be exposed dermally to atrazine after application. Risks associated with residential exposures are expressed as Margins of Exposure (MOEs). The target MOE of 1000 or more was selected for residential exposures based on a 10x UF for intraspecies variation, and a10x UF for interspecies variation, and an additional 10x for increased sensitivity of children to atrazine, as seen in neuroendocrine effects in developmental studies. MOEs greater than 1000 for adult and children do not exceed HED's level of concern, i.e. are not of concern.

4.4.1 Handler Exposure and Risk Estimates

Homeowners handling and applying atrazine are expected to receive short-term (1 to 30 days) dermal and inhalation exposures. Intermediate-term exposures (30 days to months in duration) are not expected for homeowners applying and handling lawn care products containing atrazine.

For the purposes of incorporating short-term dermal exposures into residential risk assessments, HIARC selected an endpoint of 360 mg/kg/day for decreased body weight and food consumption (based on a NOAEL of 100 mg/kg/day multiplied by the rat/human dermal penetration factor of 3.6) from a 21-day dermal toxicity/absorption study using rabbits. This study was considered appropriate because the duration and route of exposure (21-day, dermal) match the duration and route of exposure (up to one week, dermal) in the short-term dermal risk assessment.

For the purposes of incorporating short-term inhalation exposures into residential risk assessments, the HIARC selected an endpoint for decreased body weight gain and food consumption (based on a NOAEL of 10 mg/kg/day). Short-term inhalation and dermal exposures can be combined because the two exposure pathways share a common toxic effect, i.e., decreased body weight gain and food consumption.

Exposure and risk for residential handlers (adults) were estimated in essentially the same way as for occupational workers using similar application methods. The risk estimates assume that residents wear short-sleeve shirts, short pants, shoes and socks, but no gloves or respirators, i.e., baseline protective clothing. The Standard Operating Procedures (SOPs) for Residential Exposure assessments (revised

December 1999) and the Outdoor Residential Exposure Task Force (ORETF) were both used to estimate exposure and compared. ORETF data were only available for two of the five exposure scenarios: the hose-end sprayer and the push-type spreader. All residential handler short-term dermal and inhalation MOEs exceeded 1000. The aggregate dermal + inhalation MOEs ranged from 2200 to 110,000.

Table 20a summarizes the results of the short-term exposures and risk estimates for homeowner applicators. Attachment VI contains the details of this assessment and the calculations used. Table 20b summarizes the results of exposure and risk assessments using ORETF data for comparison.

Table 20a. Residential Short-term Handler Risks to Atrazine at Baseline										
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre)	Amount Handled per Day[b] (acres)	PHED Unit Exposure		Daily Dose		MOEs		
				Dermal[c] (mg/lb ai)	Inhalation[d] (µg/lb ai)	Dermal[e] (mg/kg/day)	Inhalation[f] (mg/kg/day)	Dermal[g]	Inhal-ation[h]	Aggregate
Mixer/Loader/Applicator										
Backpack Sprayer (R1)	lawns	2	0.023	5.1	30	0.0034	0.000023	150,000	430,000	110,000
Low Pressure Handwand - Liquid Formulations (R2)	lawns	2	0.023	100	30	0.066	0.000023	7,600	430,000	7,500
Granulars with a Push Type Spreader (R4)	lawns	2	0.5	3	6.3	0.043	0.00011	8,400	95,000	7,700
Granulars with a Bellygrinder (R5)	lawns	2	0.023	110	62	0.072	0.00005	5,000	210,000	4,900

Footnotes:

a Application rates are the maximum application rates determined from EPA registered labels.

b Amount handled per day values are EPA estimates of acreage treated, as found in the Residential SOPs draft December 1997; 0.5 acre lawn or 1000 ft^2 (0.023) acre spot treatment..

c Dermal unit exposure values from Residential SOPs draft December 1997. Baseline dermal exposure assumes short pants, short sleeved shirt, and no gloves. All scenarios are considered mixer/loader/applicators.

d Inhalation unit exposure values from the Residential SOPs draft December 1997 representing a no respirator scenario.

e Dermal daily dose (mg/kg/day) = daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres/day) / body weight (70 kg adult).

f Inhalation daily dose (mg/kg/day) = inhalation unit exposure (µg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres/day) x conversion factor (1 mg/1,000 µg) / body weight (60 kg; developmental female).

g Dermal MOE = NOAEL (360 mg/kg/day based) / daily dermal dose (mg/kg/day)..

h Inhalation MOE = NOAEL (10 mg/kg/day) / daily inhalation dose (mg/kg/day).

Table 20b. Residential Short-term Handler Risks to Atrazine at Baseline (Using ORETF Unit Exposure Values)										
Exposure Scenario	Crop Type/Use	Application Rate[a] (lb ai/acre)	Amount Handled per Day[b] (acres)	ORETF Unit Exposure		Daily Dose		MOEs		
				Dermal[c] (mg/lb ai)	Inhalation[d] (µg/lb ai)	Dermal[e] (mg/kg/day)	Inhalation[f] (mg/kg/day)	Dermal[g]	Inhal-ation[h]	Aggregate
Mixer/Loader/Applicator										
Hose-end (Dial-Type) Sprayer (R3)	lawns	2	0.5	11	16	0.16	0.00027	2,300	38,000	2,200
Granulars with a Push Type Spreader (R5)	lawns	2	0.5	0.68	0.91	0.0097	0.00002	37,000	660,000	35,000

Footnotes:

a Application rates are the maximum application rates determined from EPA registered labels.

b Amount handled per day values are EPA estimates of acreage treated found in the Residential SOPs draft December 1997. Baseline dermal exposure assumes short pants, short sleeved shirt, and no gloves clothing scenario. All scenarios are considered mixer/loader/applicators.

c Dermal unit exposure values from 2 Outdoor Residential Exposure Task Force ORETF (MRID 449722-01 and ORETF Study Number OMA003) studies. Unit exposure data (geometric mean values) were analyzed in 2 EPA draft memos, one dated October 19, 2000 "*A Generic Evaluation of Homeowner Exposure Associated with Liquid Pesticide Handling and Hose-End Application to Residential Lawns"* vol 6 of 6. The other data evaluation memo was also dated October 19, 2000 "*A Generic Evaluation of Homeowner Exposure Associated with Granular Turf Pesticide Handling and Application to Residential Lawns*". Homeowner exposure was assessed in this table using a short sleeved shirt, short pants, no glove clothing scenario.

d Inhalation unit exposure values from the same ORETF studies cited in footnote c representing "no respirator" scenarios.

e Dermal daily dose (mg/kg/day) = daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres/day) / body weight (70 kg adult).

f Inhalation daily dose (mg/kg/day) = inhalation unit exposure (µg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres/day) x conversion factor (1 mg/1,000 µg) / body weight (60 kg developmental female).

g Dermal MOE = NOAEL (360 mg/kg/day) / daily dermal dose (mg/kg/day).

h Inhalation MOE = NOAEL (10 mg/kg/day) / daily inhalation dose (mg/kg/day).

4.4.2 Post Application Exposures and Risk Estimates

Post application dermal exposures to atrazine residues on lawns and golf courses after treatment with atrazine are anticipated for adults as they reenter lawns to do yard work, mow, walk, or play golf. Post application dermal exposures are anticipated for toddlers on treated lawns crawling, and playing. Incidental oral exposures are anticipated for toddlers as a result of hand-to-mouth activity, soil and turf ingestion, as well as, granule ingestion while playing on treated lawns. Inhalation exposures are not expected for adults or children reentering treated lawns and golf courses after treatment. Short-term dermal post application exposures are possible for adults, and short-term post application dermal and incidental oral exposures are possible for toddlers. Intermediate-term residential post application exposures are not anticipated for either adults or children.

For the purposes of incorporating short-term dermal exposures into risk assessments, HIARC selected an endpoint of 360 mg/kg/day for decreased body weight gain and food consumption as described above. For the purposes of incorporating short-term incidental oral exposures into risk assessments for toddlers, HIARC selected an endpoint for short-term oral exposures based on decreased body weight gain and food consumption (based on a NOAEL of 10 mg/kg/day). Short-term post application dermal and incidental exposures can be combined because of the common toxic effect between the two pathways, i.e., both the short-term dermal incidental oral effect are based on decreased body weight gain and food consumption.

Dermal postapplication exposure estimates were conducted using the mean daily postapplication residue from each of the chemical specific turf transferable residue (TTR) studies (granular and dry-flowable formulations). Dermal transfer coefficients from the revised Residential SOPs were used. The SOPs use a high contact activity based on the use of Jazzercise to represent the exposures of an actively playing child. These assumptions are expected to better represent residential exposure and are still considered to be high-end, screening level assumptions.

A total of 8 dermal postapplication exposure scenarios were evaluated. Two of these scenarios , both involving application of a liquid formulation, had short-term dermal MOEs less than 1000, for high-contact activities on turf for the child (MOE = 390) and adult (MOE=660). Residues had dissipated sufficiently by the 2nd day after treatment to raise MOEs for children to 2600 and adults to 4500. For adults golfing and mowing on treated turf, all short-term dermal MOEs exceeded 1000. Assuming <u>all</u> of the adult dermal exposures (golfing, mowing, high-contact activities) would happen in one day over 8 hours, the aggregate dermal MOE ranges from 600 to 14,000, depending on the formulation applied to the turf. This very high-end aggregate risk estimate is driven by the single adult and child 'high-contact activity' scenario of concern.

It is possible for an adult resident to apply atrazine by one of several methods to their lawn, then, later that same day, take part in activities on the lawn, such as sports. Only post-application activity would result in a risk of concern. Therefore, the aggregated dose from applying atrazine by hose-end spray and then playing on the treated lawn (the highest exposure estimates) on the same day yields an MOE of 510. This should be considered a high-end, screening level exposure estimate.
Lacking dislodgeable residue data (because children's hands may be wet and sticky and TTR data was obtained with dry wipe methods), the Residential SOPs were used to estimate incidental oral exposure for toddlers (young children) licking their fingers after touching treated turf. Therefore, the risk estimate for finger licking is based on the application rate of 2 lbs ai/acre, and formulation is not a factor. Dislodgeable foliar residue (DFR) data were provided for corn, but not for turf, therefore, HED used the DFR data for corn and normalized it for a 2 lbs ai/acre application rate to represent residues on turf for use in estimating exposure for the mouthing scenario for children. The risk estimate

(MOE) for the finger licking scenario alone was 330 while mouthing grass and soil ingestion had MOEs of 1800 and 100,000, respectively. The aggregation of all of these mouthing activities (finger licking + mouthing grass + soil ingestion) results in a MOE of 280. Incidental ingestion of atrazine granules was not aggregated with these other mouthing activities because it is considered episodic. However, all risk estimates based on a single granule ingestion were of concern with MOEs of 25 to 180 depending on the formulation.

It is considered reasonably likely that dermal and oral incidental exposures may occur in the same day for children playing on atrazine-treated lawn. However, both the short-term dermal (for the spray-treated turf) and short-term hand-to-mouth exposures have MOEs less than 1000. Aggregating the route-specific MOEs for the sprayed turf residue and hand-to-mouth exposure results in an MOE of 170, which further exceeds the level of concern.

A single label for atrazine 4L (EPA Reg. No. 829-268) permits professional application to “corn in the home garden.” As this was theonly such label use found, the potential postapplication risk to residents was not quantitatively assessed; but as the potential riskestimated for postapplication workers was low, the residential risk is also considered low. Tables 21 and 22 summarize these results.

Table 21. Residential Short-term Dermal Postapplication Risks for Atrazine (Using TTR values from liquid and granular Atrazine turf studies - MRID Nos. 449580-01, 449588-01)							
Dermal Scenarios	Application Rate (lb ai/acre)	Exposure Time (hours/day)	Short Term Risks				
			Transfer Coefficient[a] (cm^2/hr)	TTR[b] (ug/cm^2) DAT 0-1		MOEs [c]	
				GA	NC-liquid FL-granular	GA	NC-liquid FL- granular
Adult dermal turf contact liquid formulation	2	2	14,500	0.241	(NC) 1.32	3,600	(NC) 660
Adult dermal turf contact granular formulation	2	2	14,500	0.0585	(FL) 0.216	15,000	(FL) 4,000
Child dermal turf contact liquid formulation	2	2	5,200	0.241	(NC) 1.32	2,200	(NC) 390
Child dermal turf contact granular formulation	2	2	5,200	0.0585	(FL) 0.216	8,900	(FL) 2,400
Adult walking, playing golf liquid formulation	2	4	500	0.241	(NC) 1.32	52,000	(NC) 9,500
Adult walking, playing golf granular formulation	2	4	500	0.0585	(FL) 0.216	220,000	(FL) 58,000
Adult push mowing lawn liquid formulation	2	2	500	0.241	(NC) 1.32	100,000	(NC) 19,000
Adult push mowing lawn granular formulation	2	2	500	0.0585	(FL) 0.216	460,000	(FL) 120,000
Aggregate Daily Dermal Risk: Adult (All Activities Listed): Liquid Formulation[f]						3,300	600
Aggregate Daily Dermal Risk: Adult (All Activities Listed): Granular Formulation[f]						14,000	3,600

a Transfer coefficient from proposed changes to the Residential SOP's (12/99).

b TTR source: liquid and granular turf studies MRID # 449580-01, 449588-01, DAT 0-1 residue. The highest residue value occurring immediately following application to DAT 1 was used for determination of DAT 0-1 MOE's. The highest residue values were detected after liquid application of a 90 DF formulation. The 90 DF study was conducted using an application rate of 2 lb ai/acre.

c MOE = Short-term NOAEL (360 mg/kg/day; based on a dermal study) / dermal dose where dermal dose = TTR (µg/cm^2) x TC (cm^2/hr) x conversion factor (1 mg/1,000 µg) x exposure time (2 hrs/day) / body weight (70 kg adult or 15 kg 1- to 6-year-old).

d TTR source: liquid and granular turf studies MRIDs # 449580-01, 449588-01, DAT 7 residue.

e MOE = Intermediate-term NOAEL (1.8 mg/kg/day; based on an oral study) / absorbed dermal dose where absorbed dose = TTR (µg/cm^2) x TC (cm^2/hr) x conversion factor (1 mg/1,000 µg) x exposure time (2 hrs/day) x dermal absorption (6%) / body weight (60 kg developmental female or 15 kg child (1-6 year old)).

f Aggregate MOE may be obtained by dividing NOAEL by sum of daily dermal doses, or by taking the inverse of the sum of the inverses of the MOEs:
Aggregate MOE = $1/[\ 1/MOE_1 + 1/MOE_2$ etc.]

Table 22. Residential Short-term Oral Nondietary Postapplication Risks to Children (1-6) from "Hand-to-Mouth" and Ingestion Exposure When Reentering Lawns Treated with Granular or Liquid Atrazine Formulations

Type of Exposure	Application Rate[a] (lb ai/acre)	Ingestion Rate or Other Assumptions[b]	Oral Dose[d] (mg/kg/day)	MOE[e]
Hand to Mouth Activity ("finger licking")	2 liquid or granular	20 cm^2/event surface area of 1-3 fingers; 20 events/hr; 5% of ai dislodgeable with potentially wet hands; 50% saliva extraction factor	0.030 (both formulations)	330
Turfgrass/Object Mouthing	2 liquid or granular	25 cm^2/day of turf; Corn DFR normalized to 2 lb ai/acre = 3.4 µg/cm^2	0.0057	1,800
Ingestion of Soil	2 liquid or granular	100 mg/day ingestion; 0.67 cm^3/gm soil	1.0E-4	100,000
Aggregate of the Oral Exposures Above[f]			0.036	280
Ingestion of Granules	0.42% ai	0.2-0.4 g/day (100-200 lbs formulation /acre)	0.056-0.11	90-180
	1.5% ai		0.2-0.4	25-50

Footnotes:

a Application rates represent maximum label rates from current EPA registered labels.

b Assumptions from Residential SOP's (December, 1999). Several assumptions used in calculating the hand to mouth activity scenario involve proposed changes to the Residential SOPs (12/99).

c TTR source: liquid and granular atrazine turf studies MRID Nos. 449580-01; 449588-01. Short-term risks assessed using DAT 0-1 residue values and intermediate-term risks assessed using DAT 7 residue values.

d Oral doses calculated using formulas presented in the Residential SOPs (December, 1999). Short-term and intermediate-term doses were calculated using the following formulas. Intermediate term doses were each multiplied by the estimated fraction of atrazine residue remaining on DAT 7 after application. An estimated 17 % of the initial DAT 0-1 residue remained after 7 days, based on the mean of the average values from 4 test sites reported in the studies (i.e., 2 test sites for the liquid formulation and 2 for the granular formulation. MRIDs 449580-01; 449588-01)

Hand-to-mouth; oral dose to child (1-6 year old) on the day of treatment (mg/kg/day) = [application rate (lb ai/acre) x fraction of residue dislodgeable with potentially wet hands (5%) x 11.2 (conversion factor to convert lb ai/acre to µg/cm^2)] x median surface area for 1-3 fingers (20 cm^2/event) x hand-to-mouth rate (ST: 20 events/hour; IT: 9.5 events/hour) x 50% saliva extraction factor x exp. time (2 hr/day) x 0.001 mg/µg / bw (15 kg child). This formula is based on proposed changes to the December 1999 Residential SOPs.

Grass/object mouthing; oral dose to child (1-6 year old) on the day of treatment (mg/kg/day) = DFR from corn DF study normalized to 2 lb ai/acre = 3.4 µg/cm^2) x ingestion rate of grass (25 cm^2/day) x .001 mg/µg / bw (15 kg child).

Soil ingestion; oral dose to child (1-6 year old) on the day of treatment (mg/kg/day) = [(application rate (lb ai/acre) x fraction of residue retained on uppermost 1 cm of soil (100% or 1.0/cm) x 4.54E+08 µg/lb conversion factor x 2.47E-08 acre/cm^2 conversion factor x 0.67 cm^3/g soil conversion factor) x 100 mg/day ingestion rate x 1.0E-06 g/µg conversion factor] / bw (15 kg). Short term dose based residue on the soil on day of application.

Granular pellet ingestion: (mg/kg/day) oral dose to child (1-6 year old) = [Granule ingestion rate (0.2-0.4 g/day) x Fraction of ai of granule formulations x 1,000 mg/g] / bw (15 kg).

Intermediate-term doses were calculated using these formula

e Oral MOE = Oral NOAEL (10 mg/kg/day for both short- and intermediate-term assessments) / Oral Dose (mg/kg/day). Oral NOAEL determined from a rat study. MOEs are reported to two significant figures; target MOE is at least 1,000.

f Aggregate MOE may be obtained by dividing oral NOAEL by sum of oral doses, or by taking the inverse of the sum of the inverses of the MOEs:

Aggregate MOE = $1/[\ 1/MOE_1 + 1/MOE_2$ etc.]

Uncertainties and Data Gaps:

These risk estimates are considered to be conservative. While uncertainty cannot be completely removed from any pesticide risk assessment, there is a substantial amount of actual field monitoring data for occupational handlers of atrazine in the largest area of use, field crops. The studies support the handler exposure and risk estimates stated here, given that most of the estimates are for typical-to-high application rates and acreage per day. Less data were available for most of the other crops and the fertilizer admixture scenarios. The postapplication risk estimates for field crops and turf are based on acceptable guideline field residue study data and are therefore of high confidence. Most of the remaining occupational postapplication risk estimates were extrapolated from those residue studies using the best available crop-specific transfer coefficients, but are considered more uncertain because of the translation of residue data from one crop to another.

Residential handler exposure and risk estimates were conducted using two sets of surrogate chemical data: the ORETF study data and the Residential SOPs. These data sets have not yet been fully compared, and therefore there are significant uncertainties in the risk estimates. Dermal postapplication exposures to atrazine were based on the higher average daily residues from the chemical-specific TTR study data, but also used standard assumptions for transfer coefficients. Oral ingestion scenarios are based on standard assumptions and formulae (Residential SOPs) which are designed to be screening level. Granular ingestion is considered episodic in nature and therefore not aggregated.

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

Aggregate risk assessments have been conducted for acute, short-term, and intermediate-term to chronic exposures to atrazine and the chlorinated metabolites. The acute aggregate risk assessment combines exposures to atrazine and the chlorinated metabolites in food and drinking water. The short-term aggregate risk assessment combines exposures to atrazine and the chlorinated metabolites in food and drinking water with residential exposures to atrazine, *per se*, anticipated to occur between 1 and 30 days after use of atrazine products at home. The intermediate-term and chronic aggregate risk assessment combines exposures to atrazine and the chlorinated metabolites in food and drinking water, only, because intermediate-term (30 days to several months) and chronic (several months to lifetime) exposure scenarios for the registered residential uses of atrazine are not expected.

The risk estimates for combined exposures to atrazine residues in food, drinking water, and through home uses presented in this document are deterministic and are based on the assumptions and "reciprocal MOE" method as described in HED SOP 99.5.[4] An uncertainty factor of 1000 has been applied across all exposure routes in the aggregate risk estimates.

a. Acute Aggregate Exposure and Risk Estimates

The aggregate risk assessment for acute exposures to atrazine and the chlorinated metabolites combines high-end one-day exposures through food and drinking water, only. HED does not anticipate high-end exposures through food, drinking water, and residential use all occurring on the same day. Therefore, acute aggregate risk estimates are the same as those presented for acute

[4] "Standard Operating Procedure (SOP) for Incorporating Estimates of Drinking Water Exposure into Aggregate Risk Assessments", HED, August 1, 1999.

drinking water risks. Exposure to atrazine from food sources (based on refined exposure estimates) and drinking water (based on surface and ground water monitoring data on finished drinking water) do not exceed HED's level of concern for acute dietary risk for any relevant subgroup, as described previously under the section for drinking water risk estimates.

b. Intermediate-term and Chronic Aggregate Exposure and Risk Estimates

The aggregate risk assessment for intermediate-term and chronic exposures to atrazine and the chlorinated metabolites combines estimates of high-end seasonal or long-term average exposures, respectively, to atrazine through drinking water with long-term average exposures through food. Neither intermediate-term nor long-term (chronic) exposures are expected to occur in the home from residential uses of atrazine. Therefore, intermediate-term and chronic aggregate risk estimates are the same as those presented for intermediate-term and chronic drinking water risks. Based on both a national deterministic assessment and a deterministic assessment for individuals with high-end exposures, HED has no concern for chronic effects associated with long-term average exposures to combined residues of atrazine plus its chlorinated metabolites in drinking water from CWS using surface water for any adult (male and female) population subgroup. One CWS in 1993 had an intermediate-term to chronic exposure based on a seasonal mean concentration of 62 ppb, which exceeded HED's level of concern for adults and children. This seasonal mean concentration is the highest measured concentration of atrazine and the chlorinated metabolites from 1993 to 1998 in the available database. Since that time, this CWS, and all other CWS for the period 1993 to 1998, have had seasonal mean concentrations below chronic DWLOC values for all adult population subgroups.

However, regardless of which default assumptions are used in the deterministic exposure assessment for drinking water, infants and/or children's subgroups are potentially at risk from exposures to combined residues of atrazine plus its chlorinated metabolites in 24 CWS using surface water. Although the risk assessment is based on a toxic endpoint which is relevant to menstruating females, only, it is indicative of alterations of the hypothalamic/pituitary/gonadal axis, which may occur in the offspring and adults of other species (humans), and it is the most sensitive endpoint available from the toxicity database, and therefore, is protective of other adverse effects.

These 24 CWS are monitored under the SDWA for atrazine. These 24 CWS represent variously 0.11% of all CWS monitoring for atrazine under the SDWA using either surface or groundwater or a blend, 0.5% of the 4886 CWS using surface water, and 0.65% of the 3670 CWS using surface water with data on atrazine residues. Under this deterministic assessment, these 24 CWS have been identified for probabilistic risk assessment. Probabilistic assessments using all available distributional data on drinking water residues, body weights, and drinking water consumption would reduce the uncertainty associated with these risks estimated deterministically.

c. Short-Term Aggregate Exposure and Risk Estimates

Short-term estimates of aggregate risk for adults applying atrazine products combines exposures through the dermal, dietary (food and drinking water), and inhalation routes. Short-term estimates of aggregate risk for post application exposures of adults combine dietary exposures (food and drinking water) and post application dermal exposures after lawn treatments. Short-term estimates of aggregate risk for post application exposures of toddlers combine dietary exposures (food and drinking water) with post application dermal and incidental oral exposures after lawn treatments. Short-term aggregate risk estimates inclusive of residential exposures are only applicable for those regions of the country where atrazine is used on turf grass, generally the Southeast and Florida.

For the purposes of aggregating short-term dermal, inhalation, and incidental oral exposures with oral dietary exposures (including food and drinking water), the HIARC selected endpoints for dermal (360 mg/kg/day), inhalation (10 mg/kg/day), and incidental oral (10 mg/kg/day) exposures based on decreased body weight gain and food consumption. For the purposes of aggregating short-term oral dietary exposures into the aggregate short-term risk assessment, HIARC selected an endpoint for decreased body weight gain and food consumption based on a NOAEL of 10 mg/kg/day. Short-term oral (dietary and incidental), inhalation and dermal exposures can be combined because of a common toxic effect between all exposure pathways, i.e., decreased body weight gain and food consumption.

The theoretical upper limit in drinking water for short-term exposures is referred to as a short-term DWLOC and is based on exposure estimates for adults and children from average residues of atrazine in food and exposure to high-end atrazine residues during application or immediately after application of atrazine to lawns. Measured concentrations of atrazine residues in surface water and groundwater from monitoring data (as presented earlier in this document) were compared to the short-term DWLOCs calculated for adults and children. If the short-term DWLOC values are greater than the measured average concentrations for atrazine residues in surface water and groundwater, there is no concern for short-term aggregate exposures to atrazine residues through food, drinking water, and home uses.

Short-term Aggregate Risk Estimates for Adult Handlers

Table 23 summarizes the results of HED's aggregate risk assessment for short-term exposures of adults applying atrazine products to the lawn and garden. Aggregate short-term DWLOC values are presented for combined dermal, inhalation and oral (dietary) exposures as these exposures have a common toxic effect, decreased body weight gain and food consumption. Measured high-end concentrations of atrazine residues in finished drinking reach a maximum daily to weekly concentration of 89 ppb, and a maximum seasonal (3 month) average concentration of 62 ppb, and maximum annual average concentrations of 20 ppb. As can be seen in Table 23, calculated short-term DWLOC values for adults (male and female) are greater than the measured maximum daily, weekly, and seasonal concentrations of atrazine residues in surface water and groundwater for all 5 application scenarios. Therefore, short-term aggregate exposures of adult handlers to atrazine residues from the specified lawn treatments do not exceed HED's level of concern. Short-term DWLOC values for adult handlers are based on a female body weight of 60 kg.

Table 23. Aggregate DWLOCs based on High-End Residential Handler Short-Term Exposures for Adults (Male and female) Making Applications @ 2 lbs ai/acre (Maximum) to Lawns

Exposure Scenario	Dietary Exposure (mg/kg/day)	Dermal Exposure (mg/kg/day)	Inhalation Exposure (mg/kg/day)	ST DWLOC (ppb)
Backpack Sprayer	0.000003	0.0034	0.000023	296
Low Pressure Hand wand	0.000003	0.066	0.000023	244
Hose-end Sprayer	0.000003	0.16	0.00027	158
Granular with Push-type Spreader	0.000003	0.0097	0.00002	291
Granular with a Belly grinder	0.000003	0.072	0.00005	238

Short-term Aggregate Risk Estimates for Toddlers'Post Application Exposures

Aggregate risk estimates for short-term exposures of toddlers playing on atrazine-treated lawns exceed HED's level of concern. HED's aggregate risk assessment for short-term exposures of toddlers playing on atrazine-treated lawns immediately after application is based on the results of the short-term post application incidental oral exposure and risk assessment for toddlers. Although dermal, inhalation, dietary, and incidental oral exposures could be combined for toddlers' post application exposures, HED notes that toddlers' exposures from individual and aggregated pathways for incidental oral exposures already exceed HED's levels of concern; i.e., a MOE of 280 for combined exposures from hand licking, grass and soil ingestion activities by toddlers, and MOEs from 25 to 180 for incidental ingestion of atrazine granules by toddlers. Toddlers' short-term dermal exposures also have MOEs less than 1000. Therefore, any addition (or aggregation) of exposures through the dermal, inhalation or dietary (food and drinking water) pathways with the incidental oral exposures would result in risk estimates that further exceed HED's level of concern for toddlers. Because short-term dermal and incidental oral post application exposure scenarios exist, which separately result in MOEs less than 1000, HED has not aggregated exposures across these routes for toddlers.

Short-term Aggregate Risk Estimates for Adults' Post Application Exposures

Table 24 summarizes the results of HED's aggregate risk assessment for short-term exposures of adults playing on atrazine-treated lawns immediately after application. These estimates of risk combine dermal and oral (dietary) exposures because short-term dermal and dietary exposures have a common toxic effect, decreased body weight gain and food consumption.

Table 24. Aggregate DWLOCs Based on High-end Residential Post application Short-Term Exposures for Adults on Treated Turf Grass

Type of Exposure	Formulation/Application Rate (lbs ai/acre)	Dermal Exposure (mg/kg/day)	Dietary Exposure* (food)(mg/kg/day)	ST DWLOC* (ppb)
Dermal Contact	2 lb ai/acre (liquid)	0.55	0.000003	zero
	2 lb ai/acre (granular)	0.09	0.000003	225
Dermal Contact Walking/Playing Golf	2 lb ai/acre (liquid)	0.038	0.000003	268
	2 lb ai/acre (granular)	0.0062	0.000003	295
Dermal Contact Pushing lawn Mower	2 lb ai/acre (liquid)	0.019	0.000003	284
	2 lb ai/acre (granular)	0.003	0.000003	297

The exposure scenario for adults playing on lawns treated with liquid formulations of atrazine results in aggregate risk estimates exceeding HED's level of concern. The short-term DWLOC for this scenario is zero. Because measured average concentrations of atrazine residues in drinking water are greater than zero, risk estimates for adults' short-term aggregate exposures under this scenario exceed HED's level of concern. All other adult post application exposure scenarios result in short-term aggregate risk estimates that do not exceed HED's level of concern. It can be seen that short-term DWLOC values for adults are greater than measured maxima, seasonal average, or annual average concentrations values of atrazine residues in drinking water for the exposure scenarios for playing golf, and mowing lawns. Aggregation of any of these activities with the exposure scenario for adults playing on treated lawns result in risk estimates that further exceed HED's level of concern. Short-term DWLOC values for adult post application exposures are based on a female body weight of 60 kg.

6.0 DATA REQUIREMENTS/LABEL CHANGES

There are no major data gaps for atrazine. The additional studies and information given below will help

to refine the risk estimates and clarify uncertainties.

Toxicity Data

There are no data gaps for atrazine. However, the HIARC has required that a 870.3800 Reproduction and Fertility Effects study be performed with the atrazine metabolite diaminochlorotriazine (DACT) - a mammalian metabolite of both atrazine and simazine. Otherwise there are no data gaps for atrazine, or the atrazine metabolites listed in this document, according to the OPPTS Series 870 Guideline requirements.

Residue Chemistry

Additional data on limited field rotational crops (OPPTS 860.1900), storage stability (OPPTS 860.1380), and an analytical method (OPPTS 860.1340) for the hydroxy metabolites of atrazine are required. The details of these data requirements can be found in Attachment IV. Tolerances for the hydroxy metabolites of atrazine are required.

Drinking Water

Additional data on atrazine's chlorinated metabolites in CWS using groundwater would help to refine risk estimates for populations obtaining their drinking water from these CWS. Additional sampling in those eight rural wells identified as having residues of concern for chronic effects based on a single sample would help to refine risk estimates for populations obtaining their drinking water from these rural wells.

In addition, HED recommends that probabilistic exposure assessments for the 25 CWS using surface water identified as having atrazine residues of concern be conducted using all available distributions of data on drinking water consumption and body weights, and residue data on atrazine plus the chloro-metabolites specific to these CWS. In particular, the following four CWS seem to have the highest concentrations of atrazine and the chlorinated metabolites: Salem (IL), Gillespie (IL), Palmyra-Modesto (IL), and Shipman (IL). These four CWS should be considered initially in any probabilistic risk assessment.

Occupational/ Residential

Additional exposure and use data on the mixing, loading and application of dry and liquid fertilizers both commercially (including cooperatives) and on-farm would help to refine risk estimates for this exposure scenario and clarify uncertainties. Probabilistic risk assessments for those residential scenarios with risk estimates exceeding HED's level of concern are recommended to refine the risk estimates and clarify uncertainties.